Supporting Information

(Hexafluoroacetylacetonato)copper(I)–cycloalkyne complexes as protected cycloalkynes

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Contents

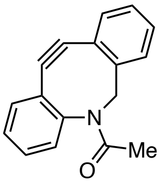
General Remarks

All reactions were performed in a dry glassware under atmosphere of argon otherwise noted. Analytical thin-layer chromatography (TLC) was performed on precoated (0.25 mm) silica-gel plates (Merck Chemicals, Silica Gel 60 F_{254}, Cat. No. 1.05715). Column chromatography was conducted using silica-gel (Kanto Chemical Co., Inc., Silica Gel 60N, spherical neutral, particle size 40–50 μm, Cat. No. 37563-85 or particle size 63–210 μm, Cat. No. 37565-85). Preparative thin-layer chromatography (PTLC) was performed on silica-gel (Wako Pure Chemical Industries Ltd., Wakogel B5-F, Cat. No. 230-00043). Melting points (Mp) were measured on a YANACO MP-J3 instrument or an OptiMelt MPA100 (Stanford Research Systems), and are uncorrected. ^{1}H and ^{13}C NMR spectra were obtained with a Bruker AVANCE 500 spectrometer at 500 or 126 MHz, respectively. ^{19}F NMR spectra were obtained with a Bruker AVANCE 400 spectrometer at 376 MHz. Chemical shifts (δ) are given in parts per million (ppm) downfield from $(CH_3)_4Si$ (δ 0.00 for ^{1}H NMR in $CDCl_3$) or the solvent peak (δ 77.0 for ^{13}C NMR in $CDCl_3$) as an internal reference or α,α,α-trifluorotoluene (δ −63.0 ppm for ^{19}F NMR in $CDCl_3$) as an external standard with coupling constants (*J*) in hertz (Hz). The abbreviations s, d, t, q, m, and br signify singlet, doublet, triplet, quartet, multiplet, and broad, respectively. IR spectra were measured by diffuse reflectance method on a Shimadzu IRPrestige-21 spectrometer attached with DRS-8000A with the absorption band given in cm^{-1}. High-resolution mass spectra (HRMS) were measured on a Bruker micrOTOF mass spectrometer under positive electrospray ionization (ESI^{+}) conditions. Elemental analyses were carried out at A Rabbit Science Japan Co., Ltd.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. [Bis(trimethylsilyl)acetylene](hexafluoroacetylacetonato)copper(I) ((btmsa)Cu(hfacac)) was purchased from Sigma–Aldrich Japan. 4-Methoxyphenylacetylene (**8**) was purchased from FUJIFILM Wako Pure Chemical Corporation. 5-Acetyl-5*H*,6*H*-11,12-

didehydrodibenzo[*b*,*f*]azocin (**1**),[S1] 5,6-didehydro-11,12-dihydrodibenzo[*a*,*e*]cyclooctene (**3**),[S2] methyl 4-(azidomethyl)benzoate (**5**),[S3] (1α,8α,9α)-bicyclo[6.1.0]non-4-yn-9-ylmethanol (**6**),[S4] 4,8-4-(azidomethyl)benzoyl chloride (**7**),[S5] ditosyl-4,8-diazacyclononyne (**10**),[S6] 11,12-didehydro-5,6-dihydro-dibenzo[*a*,*e*]cycloocten-5-ol (**S1**),[S2] 11,12-didehydro-5,6-dihydrodibenzo[*a,e*]cycloocten-5-yl *N*-(2-propyn-1-yl)carbamate (**S2**),[S7] (1α,8α,9α)-bicyclo[6.1.0]non-4-yn-9-ylmethyl (4-nitrophenyl)carbonate (**S3**),[S8] (1α,8α,9α)-bicyclo[6.1.0]non-4-yn-9-ylmethyl *N*-(2-propyn-1-yl)carbamate (**S4**),[S9] *N*-(2-propyn-1-yl) 3-(4-tosyl-4,8-diazacyclononyn-8-ylcarbonyl)propionamide (**S5**),[S9] and 8-(1-((1*R**,8*S**,9*R**)-bicyclo[6.1.0]non-4-yn-9-yl)-3,14-dioxo-2,7,10-trioxa-4,13-diazaheptadecan-17-oyl)-4-tosyl-4,8-diazacyclononyne (**14**)[S10] were prepared according to the reported methods.

Structures of Cycloalkynes



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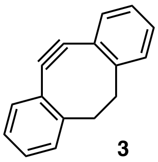

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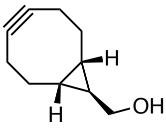

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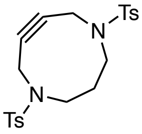

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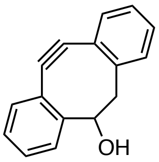

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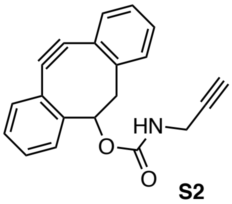

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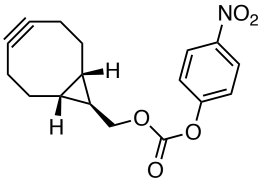

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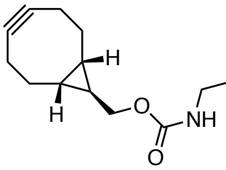

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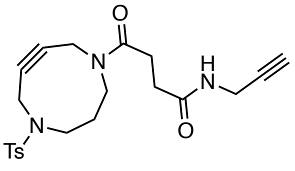
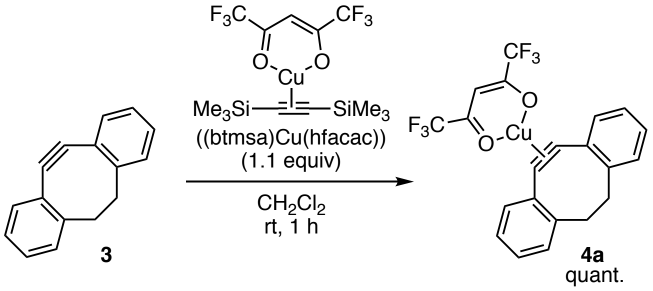


S5

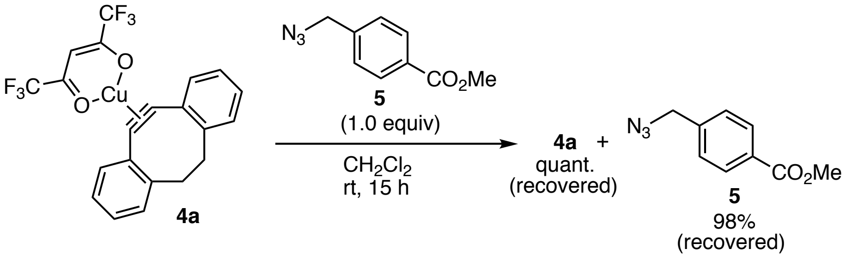
Experimental Procedures

A typical procedure for the synthesis of (hexafluoroacetylacetonato)copper(I)–cycloalkyne complexes



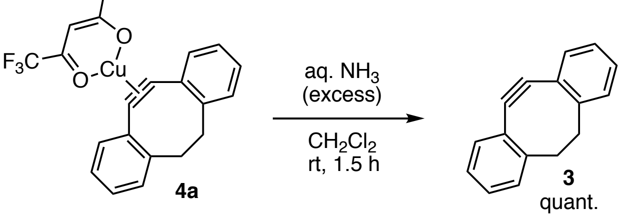
To a mixture of 5,6-didehydro-11,12-dihydrodibenzo[*a*,*e*]cyclooctene (**3**) (10.0 mg, 49.0 μmol) and [bis(trimethylsilyl)acetylene](hexafluoroacetylacetonato)copper(I) (24.1 mg, 54.6 μmol) was dissolved in dichloromethane (0.50 mL) at room temperature. After stirring for 2 h at the same temperature, the mixture was dried under reduced pressure. The residue was purified by flash column chromatography (silica-gel 1.0 g, *n*-hexane/EtOAc = 20/1) to give copper(I)–cycloalkyne complex **4a** (23.2 mg, 49.0 μmol, quant.) as a colorless solid.

*Examination of SPAAC reactivity of (hexafluoroacetylacetonato)copper(I)–cycloalkyne complex **4a** with azide **5***



To a solution of copper(I)–cycloalkyne complex **4a** (47.4 mg, 99.9 μmol) dissolved in dichloromethane (1.0 mL) was added methyl 4-(azidomethyl)benzoate (**5**) (19.1 mg, 99.9 μmol) at room temperature. After stirring for 15 h at the same temperature, the mixture was dried under reduced pressure. To the residue was added 1,1,2,2-tetrachloroethane (8.40 mg, 50.0 μmol) as an internal standard. After dissolving the mixture in $CDCl_3$, ^1H NMR analysis (400 MHz) was performed. This result determined the yields of copper(I)–cycloalkyne complex **4a** (quant.) and azide **5** (98%) by comparing the relative values of integration for the peaks observed at 3.40 ppm (s, 2H, for **4a**) and 4.42 ppm (s, 2H, for **5**) with that of 1,1,2,2-tetrachloroethane observed at 5.95 ppm (s, 2H).

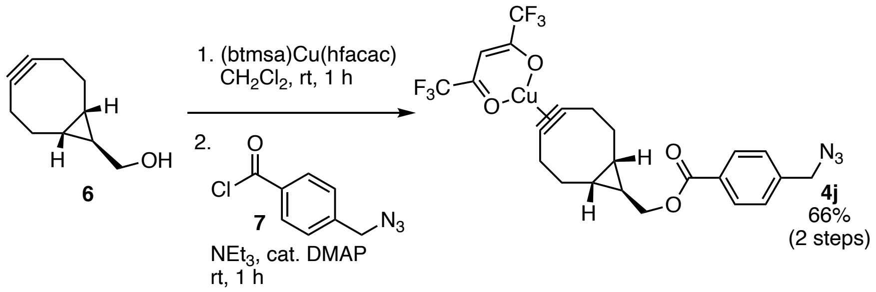
*A typical procedure for deprotection of (hexafluoroacetylacetonato)copper(I)–cycloalkyne complex **4a** with an aqueous ammonia*



To a solution of copper(I)–cycloalkyne complex **4a** (20.4 mg, 43.0 μmol) dissolved in dichloromethane (4.0 mL) was added an aqueous ammonia solution (28%, 4.0 mL) at room temperature. After stirring for 1.5 h at the same temperature, the mixture was extracted with dichloromethane (5 mL × 3). The combined organic extract was washed with brine, and then dried (Na_2SO_4). After filtration, the filtrate was concentrated under reduced pressure. The residue was through a short pad of silica-gel (1.0 g) to give 5,6-didehydro-11,12-dihydrodibenzo[*a*,*e*]cyclooctene

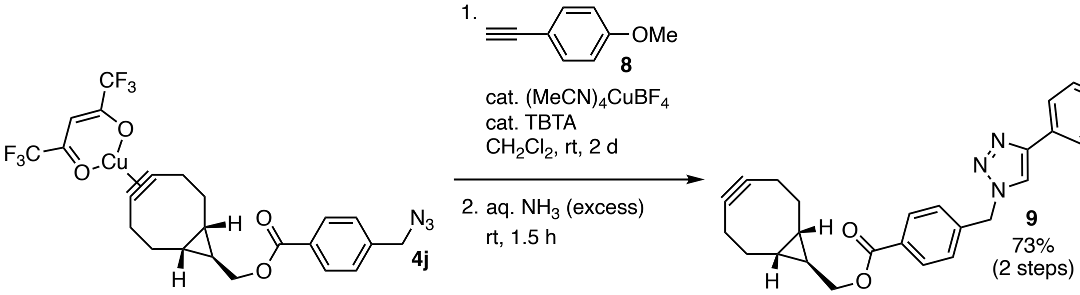
(**3**) (8.95 mg, 43.8 μmol, quant.) as a colorless solid.

*Synthesis of copper(I)–cycloalkyne complex **4j** containing an azido group*



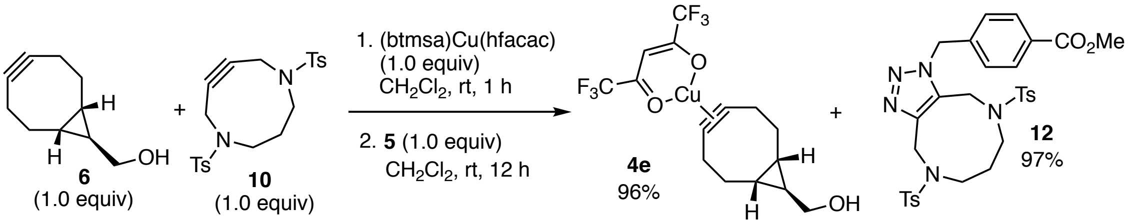
To a solution of BCN **6** (24.2 mg, 0.161 mmol) dissolved in dichloromethane (1.6 mL) was added [bis(trimethylsilyl)acetylene](hexafluoroacetylacetonato)copper(I) (77.1 mg, 0.175 mmol) at room temperature. After stirring for 1 h at the same temperature, to the mixture was added triethylamine (32.5 mg, 0.321 mmol), *N*,*N*-dimethyl-4-aminopyridine (DMAP) (0.81 mg, 6.6 μmol), and 4-(azidomethyl)benzoyl chloride (**7**) (60.5 mg, 0.309 mmol) at room temperature. After stirring for 1 h at the same temperature, to the mixture was added water. The mixture was extracted with dichloromethane (10 mL × 3), and the combined organic extract was washed with brine, and then dried (Na_2SO_4). After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography (silica-gel 5.0 g, *n*-hexane/EtOAc = 5/1 to 2/1) to give copper(I)–cycloalkyne complex **4j** (61.5 mg, 0.106 mmol, 66%) as a colorless solid.

*CuAAC reaction of copper(I)–cycloalkyne complex **4j** with alkyne **8***



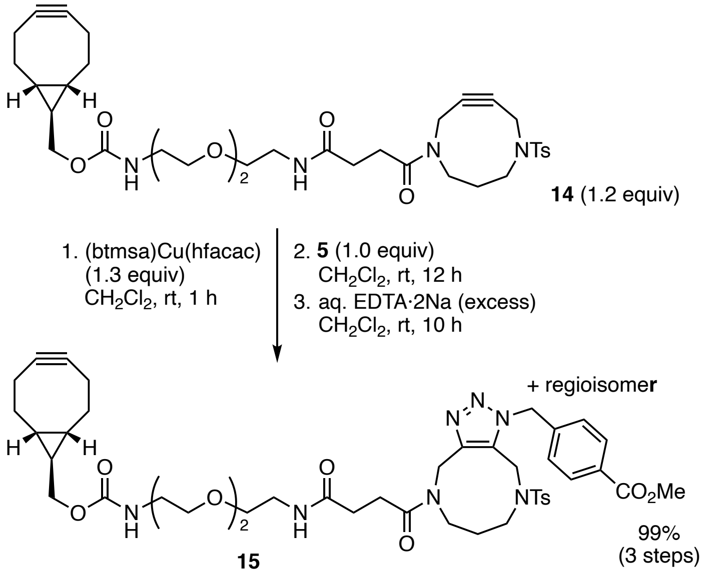
To a solution of copper(I)–cycloalkyne complex **4j** (10.5 mg, 18.0 μmol) dissolved in dichloromethane (0.40 mL) was added $(MeCN)_4CuBF_4$ (0.62 mg, 1.9 μmol), 4-ethynylanisole (2.51 mg, 19.0 μmol), and TBTA (1.01 mg, 1.90 μmol) at room temperature. After stirring for 2 d at the same temperature, to the mixture was added an aqueous ammonia solution (28%, 1.0 mL). After stirring for 1.5 h, the mixture was extracted with dichloromethane (5 mL × 3). The combined organic extract was washed with brine, and then dried (Na_2SO_4). After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (*n*-hexane/EtOAc = 1/1) to give cyclooctyne **9** (5.80 mg, 13.2 μmol, 73%) as a colorless amorphous.

*Typical procedure for the competition reaction in the cycloaddition with azide **5** via complexation with copper*



To a mixture of BCN **6** (5.26 mg, 35.0 μmol) and DACN **10** (14.3 mg, 33.1 μmol) dissolved in dichloromethane (0.70 mL) was added [bis(trimethylsilyl)acetylene](hexafluoroacetylacetonato)copper(I) (14.8 mg, 34.8 μmol) at room temperature. After stirring for 1 h at the same temperature, to the mixture was added methyl 4-(azidomethyl)benzoate (**5**) (6.89 mg, 36.0 μmol) in dichloroethane (0.70 mL). After stirring for 12 h, the mixture was dried under reduced pressure. To the residue was added 1,4-dinitrobenzene (10.6 mg, 63.2 μmol) as an internal standard. After dissolving the mixture in $CDCl_3$, ^1H NMR analysis (400 MHz) was performed. This result determined the yields of copper(I)–cycloalkyne complex **4e** (96%) and triazole **12** (97%) by comparing the relative values of integration for the peaks observed at 3.56 ppm (d, 2H, for **4e**) and 5.90 ppm (s, 2H, for **12**) with that of 1,4-dinitrobenzene observed at 8.45 ppm (s, 4H).

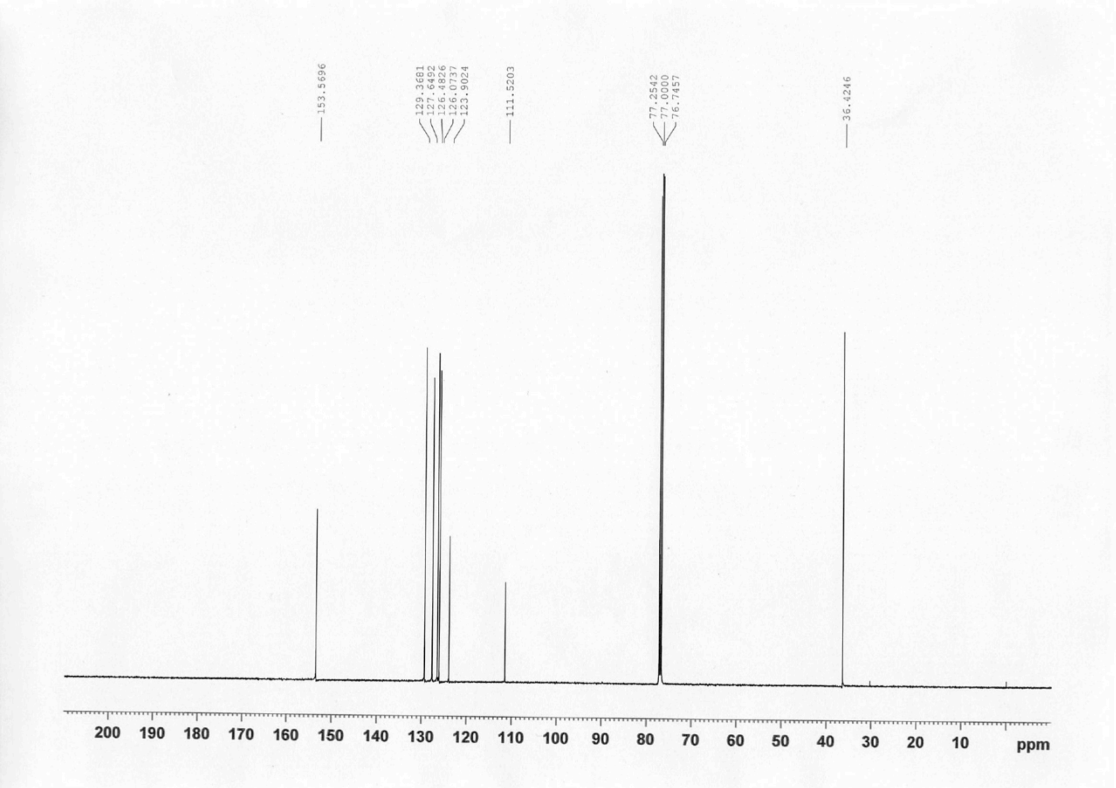
*Selective SPAAC reaction of diyne **14** via protection of bicyclo[6.1.0]nonyne moiety with copper*



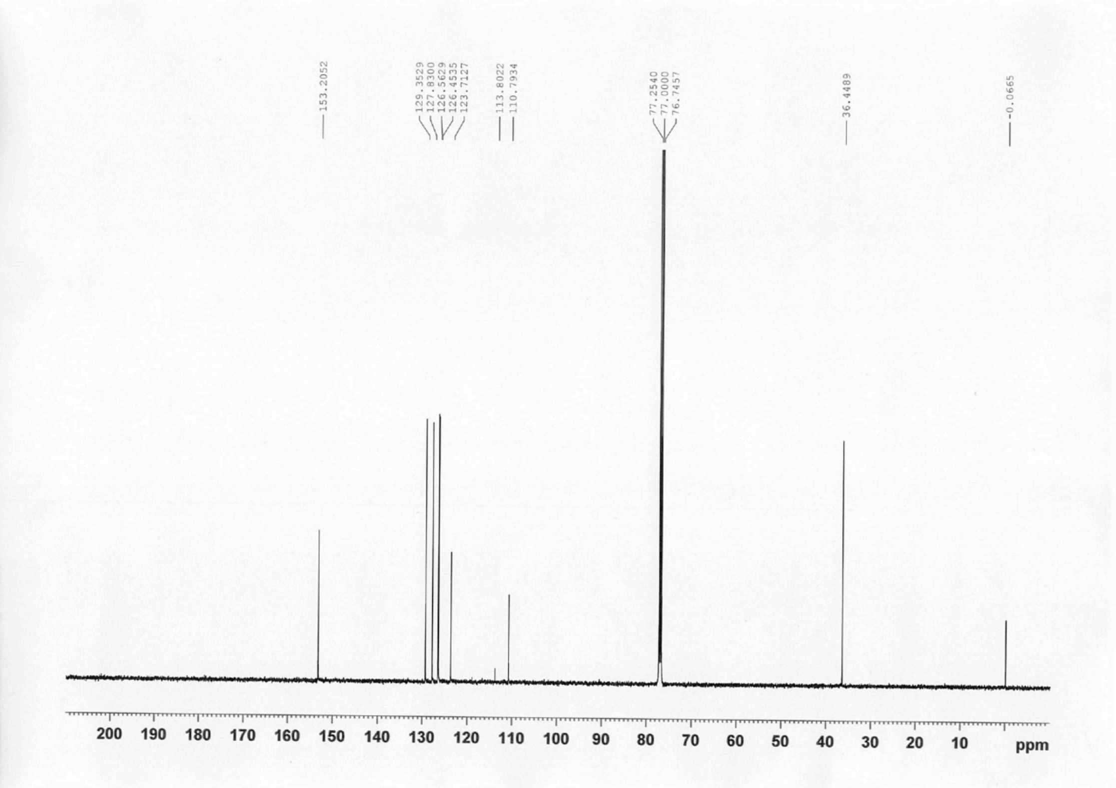
A mixture of diyne **14** (8.23 mg, 12.6 μmol) and [bis(trimethylsilyl)acetylene](hexafluoroacetylacetonato) copper(I) (6.21 mg, 14.1 μmol) was dissolved in dichloromethane (1.3 mL) at room temperature. After stirring for 1 h at the same temperature, to the mixture was added methyl 4-(azidomethyl)benzoate (**5**) (2.09 mg, 10.9 μmol) in dichloromethane (0.70 mL). After stirring for 12 h, to the mixture was added an aqueous solution of EDTA·2Na (0.2 M, 2.8 mL) and dichloromethane (3.0 mL). After stirring for 10 h, the mixture was extracted with dichloromethane (5 mL × 3). The combined organic extract was washed with brine, and then dried (Na_2SO_4). After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by preparative TLC (dichloromethane/MeOH = 20:1) to give cycloalkyne **15** (9.44 mg, 10.8 μmol, 99%) as a colorless oil.

^{13}C NMR spectra of cyclooctyne ***3*** *with or without (btmsa)Cu(hfacac) (126 MHz, $CDCl_3$) (for Fig 3C)*

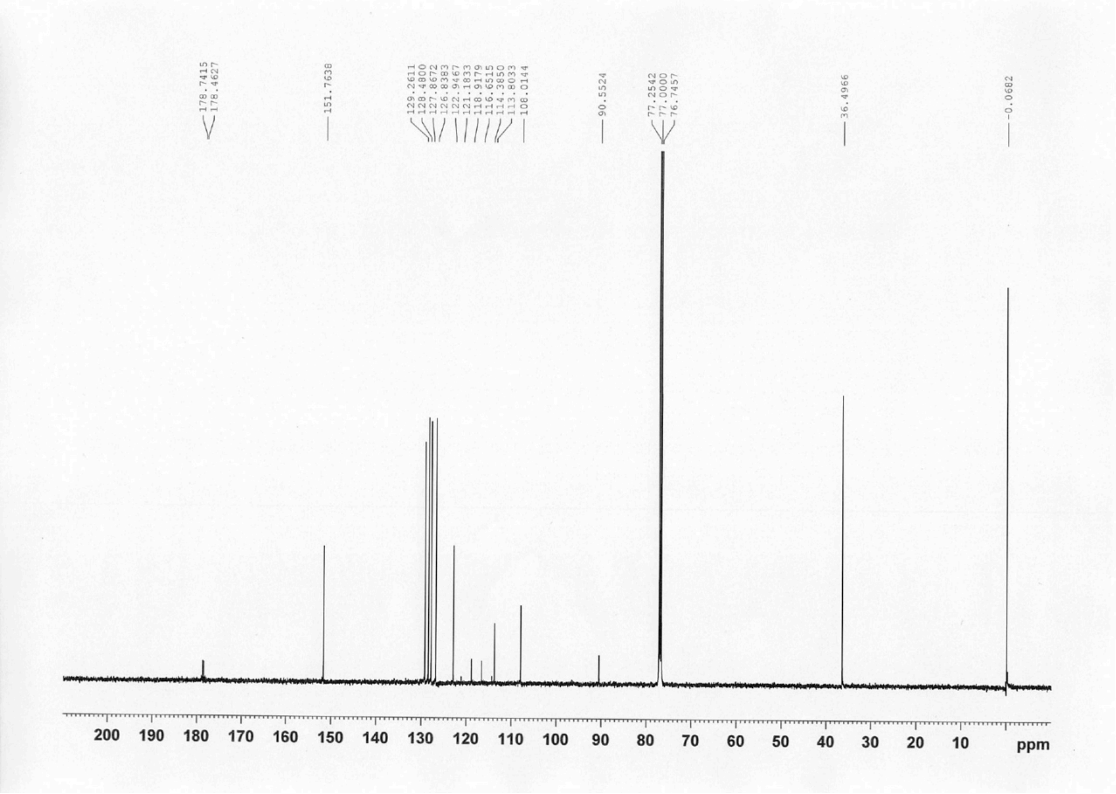
Cyclooctyne **3**



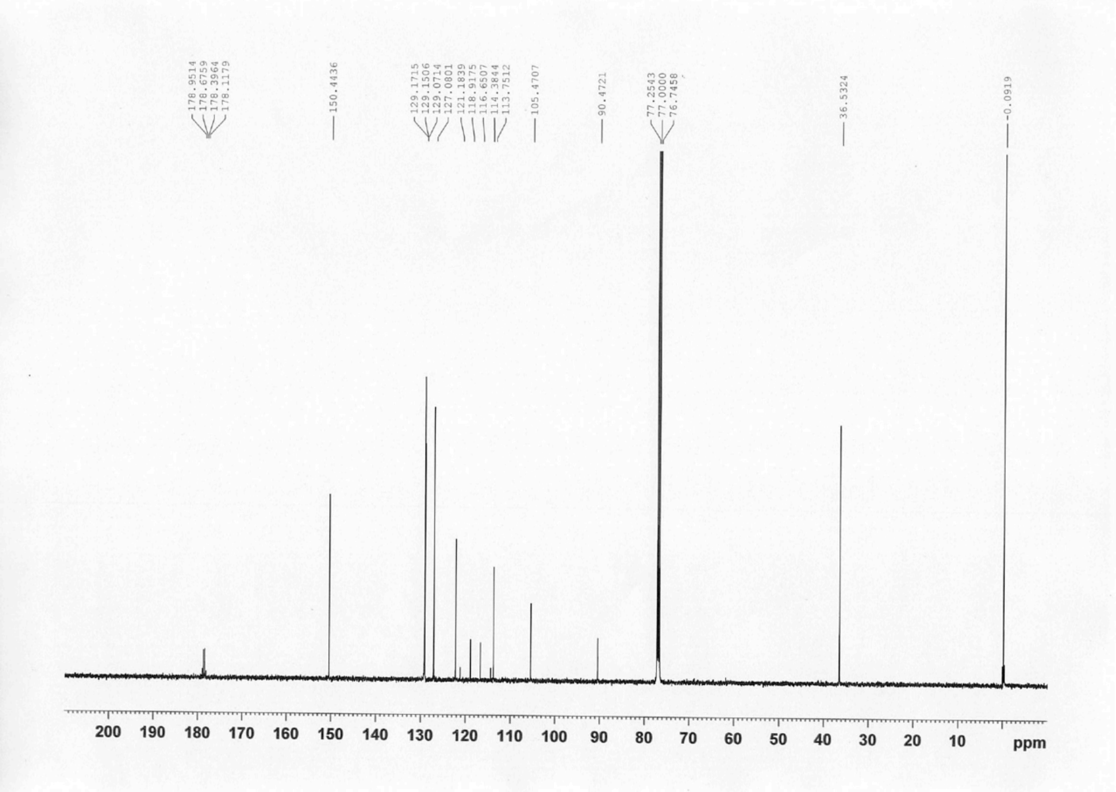
Cyclooctyne **3**:(btmsa)Cu(hfacac) = 1.0:0.10



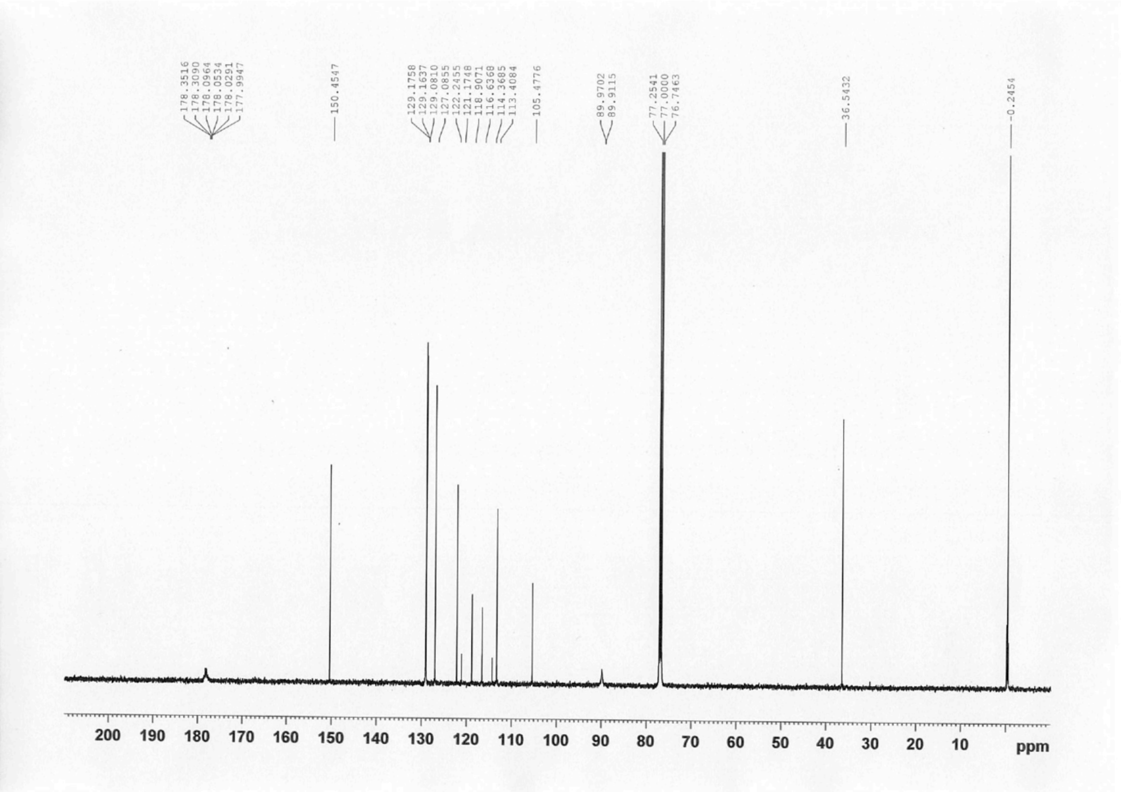
Cyclooctyne **3**:(btmsa)Cu(hfacac) = 1.0:0.50



Cyclooctyne **3**:(btmsa)Cu(hfacac) = 1.0:1.0



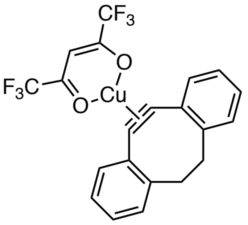
Cyclooctyne **3**:(btmsa)Cu(hfacac) = 1.0:2.0



Characterization Data of New Compounds

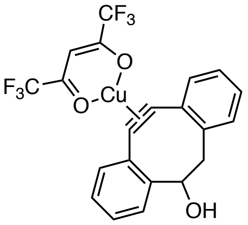
1-(6*H*-Isoindolo[2,1-*a*]indol-11-yl)ethanone (**2**),[S11] ((5a*R*,6*R*,6a*S*)-1-(4-(methoxycarbonyl)benzyl)-1,4,5,5a,6,6a,7,8-octahydrocyclopropa[5,6]cycloocta[1,2-*d*][1,2,3]triazol-6-yl)methanol (**11**),[S12] and methyl 4-((5-(1-((1*R**,8*S**,9*R**)-bicyclo[6.1.0]non-4-yn-9-yl)-3,14-dioxo-2,7,10-trioxa-4,13-diazaheptadecan-17-oyl)-9-tosyl-5,6,7,8,9,10-hexahydro-[1,2,3]triazolo[4,5-*g*][1,5]diazonin-1(4*H*)-yl)methyl)benzoate (**15**)[S10] were identical in spectra data with those reported in the literature.

[5,6-Didehydro-11,12-dihydrodibenzo[*a*,*e*]cyclooctene](hexafluoroacetylacetonato)copper(I) (**4a**)



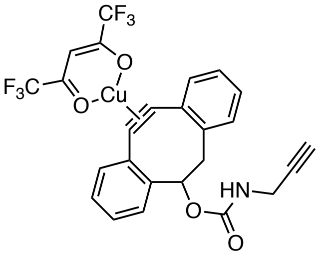
Colorless solid; Mp 155–156 °C; TLC R_f 0.37 (*n*-hexane/EtOAc = 10/1); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.37–2.45 (m, 2H), 3.37–3.44 (m, 2H), 6.31 (s, 1H), 7.30–7.38 (m, 6H), 7.69–7.71 (m, 2H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 36.5 (2C), 90.6 (1C), 105.5 (2C), 117.8 (q, 2C, J = 285.6 Hz), 122.2 (2C), 127.1 (2C), 129.1 (2C), 129.16 (2C), 129.19 (2C), 150.5 (2C), 178.6 (q, 2C, J = 35.2 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ –76.3 (s, 6F); IR (KBr, cm^{-1}) 757, 1017, 1265, 1396, 1448, 1513, 1575, 2955, 3064; Anal. calcd. $C_{21}H_{13}CuF_6O_2$: C, 53.12; H, 2.76%; Found: C, 53.31; H, 2.60%.

[11,12-Didehydro-5,6-dihydro-dibenzo[*a*,*e*]cycloocten-5-ol](hexafluoroacetylacetonato)copper(I) (**4b**)



Colorless solid; Mp 170–172 °C; TLC R_f 0.36 (*n*-hexane/EtOAc = 3/1); Compound **4b** was observed as a mixture of conformational isomers in NMR analyses; ^{1}H NMR for major isomer ($CDCl_3$, 500 MHz) δ 2.24 (d, 1H, J = 4.5 Hz), 2.85 (dd, 1H, J = 15.0, 3.2 Hz), 3.17 (dd, 1H, J = 15.0, 3.2 Hz), 4.55 (brd, 1H, J = 3.2 Hz), 6.31 (s, 1H), 7.36–7.41 (m, 4H), 7.47 (ddd, 1H, J = 7.6, 7.6, 1.0 Hz), 7.65–7.67 (m, 2H), 7.73 (d, 1H, J = 7.8 Hz); ^{13}C NMR for major isomer ($CDCl_3$, 126 MHz) δ 48.4 (1C), 75.4 (1C), 90.7 (1C), 104.7 (1C), 106.5 (1C), 117.8 (q, 2C, J = 285.5 Hz), 119.5 (1C), 122.4 (1C), 123.3 (1C), 127.4 (1C), 127.5 (1C), 129.0 (1C), 129.1 (1C), 129.3 (1C), 129.4 (1C+1C, two signals overlapped), 148.2 (1C), 152.4 (1C), 178.6 (q, 2C, J = 35.1 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ –76.0 (s, 6F); IR (KBr, cm^{-1}) 755, 1148, 1205, 1260, 1532, 1669, 3301; HRMS (ESI$^+$) *m/z* 512.9969 ([M+Na]$^+$, $C_{21}H_{13}CuF_6NaO_3^+$ requires 512.9957).

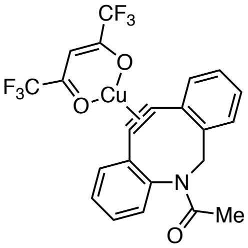
[11,12-Didehydro-5,6-dihydrodibenzo[*a,e*]cycloocten-5-yl *N*-(2-propyn-1-yl)carbamate](hexafluoroacetylacetonato)copper(I) (**4c**)



Colorless solid; Mp 184 °C (decomp.); TLC R_f 0.37 (*n*-hexane/EtOAc = 1/1); Compound **4c** was observed as a mixture of conformational isomers in NMR analyses; ^{1}H NMR for major isomer

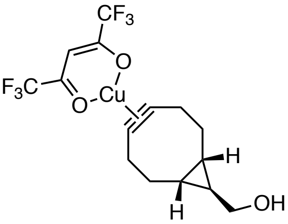
($CDCl_3$, 500 MHz) δ 2.29 (brs, 1H), 2.90 (d, 1H, J = 15.1 Hz), 3.28 (dd, 1H, J = 15.1 Hz), 3.98–4.03 (br, 2H), 5.16–5.24 (br, 1H), 5.48–5.53 (br, 1H), 6.30–6.34 (br, 1H), 7.33–7.53 (m, 6H), 7.68–7.72 (m, 2H); ^{13}C NMR for major isomer ($CDCl_3$, 126 MHz) δ 31.0 (1C), 45.9 (1C), 72.0 (1C+1C, two signals overlapped), 77.3 (1C), 90.6 (1C), 104.3 (1C), 106.7 (1C), 117.8 (q, 2C, J = 285.6 Hz), 119.5 (1C), 122.2 (1C), 123.2 (1C), 127.7 (1C), 127.8 (1C), 129.0 (1C), 129.31 (1C), 129.33 (1C), 129.5 (1C), 129.8 (1C), 147.3 (1C), 148.6 (1C), 154.7 (1C), 178.7 (q, 2C, J = 35.3 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ –76.2 (s, 6F); IR (KBr, cm^{-1}) 761, 1149, 1259, 1468, 1532, 1639, 1698, 2930, 3306; HRMS (ESI$^+$) *m/z* 594.0188 ([M+Na]$^+$, $C_{25}H_{16}CuF_6NNaO_4^+$ requires 594.0172).

[5-Acetyl-5*H*,6*H*-11,12-didehydrodibenzo[*b*,*f*]azocin](hexafluoroacetylacetonato)copper(I) (**4d**)



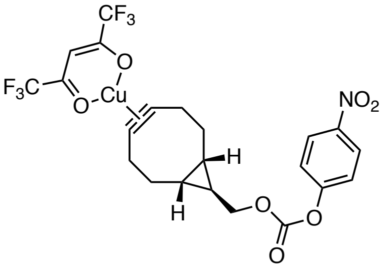
Colorless solid; Mp 165 °C (decomp.); TLC R_f 0.44 (dichloromethane); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.83 (s, 3H), 3.76 (d, 1H, J = 13.7 Hz), 5.24 (d, 1H, J = 13.7 Hz), 6.34 (s, 1H), 7.32–7.34 (m, 1H), 7.39–7.50 (m, 4H), 7.61–7.63 (m, 1H), 7.71–7.77 (m, 2H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 23.1 (1C), 55.1(1C), 90.7 (1C), 102.0 (1C), 108.3 (1C), 117.7 (q, 2C, J = 285.2 Hz), 120.5 (1C), 121.6 (1C), 128.4 (1C), 128.5 (1C), 128.6 (1C), 128.7 (1C), 129.5 (1C), 129.8 (1C+1C, two signals overlapped), 132.4 (1C), 144.2 (1C), 149.0 (1C), 170.8 (1C), 178.8 (q, 2C, J = 37.7 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ –76.2 (s, 6F); IR (KBr, cm^{-1}) 773, 1258, 1471, 1533, 1640, 1713, 1961, 2931, 3066; HRMS (ESI$^+$) *m/z* 518.0242 ([M+H]$^+$, $C_{22}H_{15}CuF_6NO_3^+$ requires 518.0247).

[(1α,8α,9α)-Bicyclo[6.1.0]non-4-yn-9-ylmethanol](hexafluoroacetylacetonato)copper(I) (**4e**)



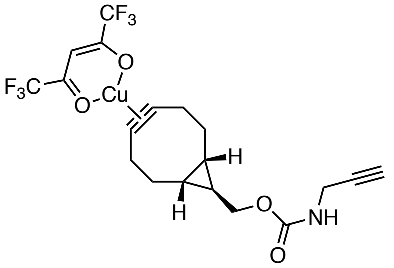
Colorless solid; Mp 143 °C (decomp.); TLC R_f 0.29 (*n*-hexane/EtOAc = 2/1); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.71–0.79 (m, 3H), 1.32 (br s, 1H), 1.44–1.53 (m, 2H), 2.38–2.42 (m, 2H), 2.56–2.64 (m, 4H), 3.56 (br s, 2H), 6.14 (s, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 21.8 (2C), 22.7 (2C), 26.9 (1C), 30.9 (2C), 66.6 (1C), 90.0 (1C), 99.3 (2C), 117.7 (q, 2C, J = 286.1 Hz), 178.0 (q, 2C, J = 34.6 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ –76.4 (s, 6F); IR (KBr, cm^{-1}) 1150, 1261, 1478, 1532, 1635, 2931, 3310; HRMS (ESI$^+$) *m/z* 443.0119 ([M+Na]$^+$, $C_{15}H_{15}CuF_6NaO_3^+$ requires 443.0114).

[(1α,8α,9α)-Bicyclo[6.1.0]non-4-yn-9-ylmethyl (4-nitrophenyl)carbonate](hexafluoroacetylacetonato)copper(I) (**4f**)



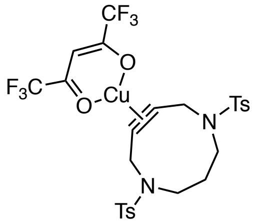
Colorless solid; Mp 145–147 °C; TLC R_f 0.26 (*n*-hexane/EtOAc = 3/1); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.87–0.95 (m, 3H), 1.49–1.53 (m, 2H), 2.42–2.45 (m, 2H), 2.61–2.66 (m, 4H), 4.23 (d, 2H, J = 6.7 Hz), 6.15 (s, 1H), 7.38–7.41 (m, 2H), 8.23–8.31 (m, 2H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 22.5 (2C+2C, two signals overlapped), 22.6 (1C), 30.6 (2C), 73.3 (1C), 90.0 (1C), 99.2 (2C), 117.7 (q, 2C, J = 286.1 Hz), 121.7 (2C), 125.3 (2C), 145.4 (1C), 152.6 (1C), 155.5 (1C), 178.1 (q, 2C, J = 34.7 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ –76.4 (s, 6F); IR (KBr, cm^{-1}) 1149, 1215, 1258, 1348, 1475, 1641, 1767, 2936; HRMS (ESI$^+$) *m/z* 608.0184 ([M+Na]$^+$, $C_{22}H_{18}CuF_6NNaO_7^+$ requires 608.0176).

[(1α,8α,9α)-Bicyclo[6.1.0]non-4-yn-9-ylmethyl *N*-(2-propyn-1-yl)carbamate](hexafluoroacetylacetonato)copper(I) (**4g**)



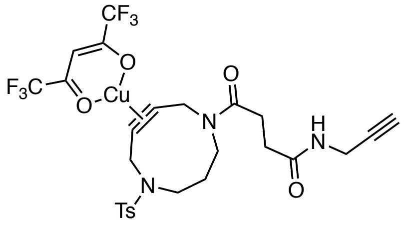
Colorless solid; Mp 166 °C (decomp.); TLC R_f 0.36 (*n*-hexane/EtOAc = 1/1); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 0.73–0.79 (m, 3H), 1.42–1.44 (m, 2H), 2.23–2.27 (br, 1H), 2.36–2.39 (m, 2H), 2.50–2.59 (m, 4H), 3.96–4.00 (m, 4H), 4.89–4.99 (br, 1H), 5.98–6.08 (br, 1H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 22.1 (2C), 22.5 (2C), 23.2 (1C), 30.7 (1C), 30.9 (2C), 69.1 (1C), 71.6 (1C), 79.5 (1C), 89.2 (1C), 98.9 (2C), 117.7 (q, 2C, J = 286.6 Hz), 156.3 (1C), 177.4 (q, 2C, J = 34.0 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ –77.2 (s, 6F); IR (KBr, cm^{-1}) 790, 1157, 1258, 1350, 1469, 1537, 1693, 1712, 2935, 3309; HRMS (ESI$^+$) *m/z* 524.0315 ([M+Na]$^+$, $C_{19}H_{18}CuF_6NNaO_4^+$ requires 524.0328).

[4,8-Ditosyl-4,8-diazacyclononyne](hexafluoroacetylacetonato)copper(I) (**4h**)



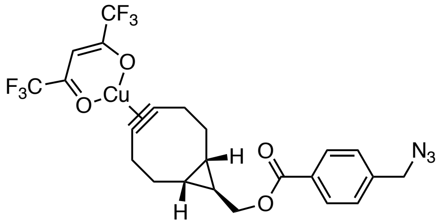
Colorless solid; Mp 172 °C (decomp.); TLC R_f 0.34 (*n*-hexane/EtOAc = 1/2); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.22–2.27 (m, 2H), 2.46 (s, 6H), 3.26–3.28 (m, 4H), 4.17 (s, 4H), 6.20 (s, 1H), 7.37–7.38 (m, 4H), 7.70–7.72 (m, 4H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 21.6 (2C), 31.7 (1C), 42.5 (2C), 45.2 (2C), 90.6 (1C), 92.5 (2C), 117.5 (q, 2C, J = 285.7 Hz), 127.5 (4C), 130.1 (4C), 133.4 (2C), 144.3 (2C), 178.6 (q, 2C, J = 35.2 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ –76.0 (s, 6F); IR (KBr, cm^{-1}) 663, 691, 889, 1159, 1196, 1256, 1355, 1534, 1641, 1671, 2966; HRMS (ESI$^+$) *m/z* 725.0253 ([M+Na]$^+$, $C_{26}H_{25}CuF_6N_2NaO_6S_2^+$ requires 725.0246).

[3-(4-Tosyl-4,8-diazacyclononyn-8-ylcarbonyl)propionamide](hexafluoroacetylacetonato)copper(I) (**4i**)



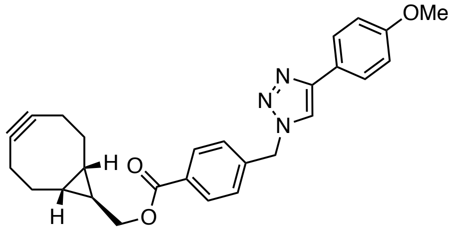
Colorless solid; Mp 162 °C (decomp.); TLC R_f 0.21 (*n*-hexane/EtOAc = 1/2); Compound **4i** is a mixture of rotamers, which were observed in NMR analyses; ^{1}H NMR for a mixture of rotamers ($CDCl_3$, 500 MHz) δ 2.17–2.22 (m, 3H), 2.45 (s, 3H), 2.52–2.59 (m, 2H), 2.67–2.71 (m, 2H), 3.12–3.14 (m, 1H), 3.25–3.27 (m, 1H), 3.59–3.66 (m, 2H), 3.96–4.02 (m, 2H), 4.11 (s, 1H), 4.15 (s, 1H), 4.37 (s, 1H), 4.51 (s, 1H), 6.11 (br s, 1H), 6.19 (s, 1H), 7.35–7.36 (m, 2H), 7.69–7.70 (m, 2H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 21.5, 28.8, 28.9, 29.1, 29.2, 30.8, 31.0, 37.7, 40.7, 41.2, 41.9, 43.5, 44.0, 45.2, 45.3, 71.4, 71.5, 79.5, 90.5, 91.9, 92.2, 92.6, 117.5 (q, J = 285.5 Hz), 127.3, 127.4, 129.9, 130.0, 134.2, 134.4, 144.1, 144.2, 171.5, 171.6, 172.5, 178.5 (q, *J* = 35.3 Hz); ^{19}F NMR (CDCl$_3$, 376 MHz) δ –76.3 (s, 6F); IR (KBr, cm^{-1}) 787, 1193, 1257, 1454, 1598, 1651, 1728, 2927, 3296; HRMS (ESI$^+$) *m/z* 708.0638 ([M+Na]$^+$, $C_{26}H_{26}CuF_6N_3NaO_6S^+$ requires 708.0635).

[((1α,8α,9α)-Bicyclo[6.1.0]non-4-yn-9-yl)methyl 4-(azidomethyl)benzoate](hexafluoroacetylacetonato)copper(I) (**4j**)



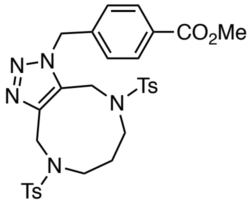
Colorless solid; Mp 128 °C (decomp.); TLC R*f* 0.50 (*n*-hexane/EtOAc = 1/1); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 0.90–0.91 (m, 3H), 1.47–1.49 (m, 2H), 2.40–2.43 (m, 2H), 2.56–2.65 (m, 4H), 4.27 (d, 2H, *J* = 6.4 Hz), 4.43 (s, 2H), 6.14 (s, 1H), 7.40–7.42 (m, 2H), 8.06–8.08 (m, 2H); ^{13}C NMR (CDCl$_3$, 126 MHz) δ 22.3 (2C), 22.6 (2C), 23.2 (1C), 30.8 (2C), 54.3 (1C), 68.7 (1C), 90.0 (1C), 99.2 (2C), 117.5 (q, 2C, *J* = 286.3 Hz), 128.0 (2C), 130.1 (2C), 130.3 (1C), 140.4 (1C), 166.2 (1C), 178.0 (q, 2C, *J* = 34.9 Hz); ^{19}F NMR (CDCl$_3$, 376 MHz) δ –76.4 (s, 6F); IR (KBr, cm^{-1}) 748, 1274, 1471, 1639, 1712, 2102, 2986, 3053; HRMS (ESI$^+$) *m/z* 602.0543 ([M+Na]$^+$, $C_{23}H_{20}CuF_6N_3NaO_4^+$ requires 602.0546).

((1α,8α,9α)-Bicyclo[6.1.0]non-4-yn-9-yl)methyl 4-((4-(4-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)methyl)benzoate (**9**)



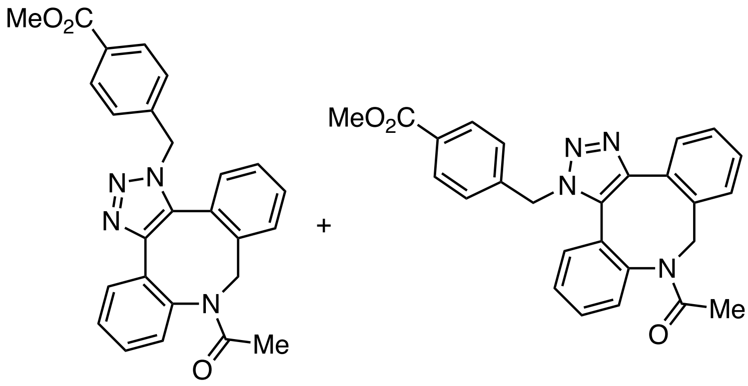
Colorless amorphous; TLC R*f* 0.42 (*n*-hexane/EtOAc = 1/1); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 0.81–0.85 (m, 3H), 1.37–1.43 (m, 2H), 2.15–2.18 (m, 2H), 2.27–2.33 (m, 2H), 2.40–2.43 (m, 2H), 3.84 (s, 3H), 4.25 (d, 2H, *J* = 6.4 Hz), 5.63 (s, 2H), 6.93–6.95 (m, 2H), 7.35–7.37 (m, 2H), 7.60 (s, 1H), 7.72–7.74 (m, 2H), 8.05–8.07 (m, 2H); ^{13}C NMR (CDCl$_3$, 126 MHz) δ 21.4 (2C), 23.1 (2C), 23.5 (1C), 33.3 (2C), 53.7 (1C), 55.3 (1C), 69.4 (1C), 98.7 (2C), 114.2 (2C), 118.7 (1C), 123.0 (1C), 127.0 (2C), 127.8 (2C), 130.4 (2C), 130.9 (1C), 139.6 (1C), 148.4 (1C), 159.7 (1C), 166.0 (1C); IR (KBr, cm^{-1}) 796, 1226, 1454, 1531, 1672, 1712, 2937, 3053; HRMS (ESI$^+$) *m/z* 442.2127 ([M+H]$^+$, $C_{27}H_{28}N_3O_3^+$ requires 442.2125).

Methyl 4-((5,9-ditosyl-5,6,7,8,9,10-hexahydro-[1,2,3]triazolo[4,5-*g*][1,5]diazonin-1(4*H*)-yl)methyl)benzoate (**12**)



Colorless oil; TLC R*f* 0.57 (*n*-hexane/EtOAc = 1/1); ^{1}H NMR (CDCl$_3$, 500 MHz) δ 1.76–1.81 (m, 2H), 2.44 (s, 6H), 2.98–3.00 (m, 2H), 3.36–3.38 (m, 2H), 3.93 (s, 3H), 4.44 (s, 2H), 4.46 (s, 2H), 5.90 (s, 2H), 7.32–7.36 (m, 6H), 7.59–7.60 (m, 2H), 7.66–7.67 (m, 2H), 8.03–8.05 (m, 2H); ^{13}C NMR (CDCl$_3$, 126 MHz) δ 21.55 (1C), 21.56 (1C), 29.1 (1C), 41.8 (1C), 47.6 (1C), 48.4 (1C), 48.7 (1C), 51.6 (1C), 52.2 (1C), 127.0 (2C), 127.3 (2C), 127.5 (2C), 130.0 (2C), 130.1 (2C), 130.3 (2C), 133.4 (2C), 135.1 (1C), 140.0 (1C), 142.9 (2C), 144.3 (1C), 144.3 (1C), 166.5 (1C); IR (KBr, cm^{-1}) 741, 1159, 1278, 1336, 1454, 1614, 1720, 2951, 3059; HRMS (ESI$^+$) *m/z* 646.1770 ([M+Na]$^+$, $C_{30}H_{33}N_5NaO_6S_2^+$ requires 646.1764).

The cycloadducts **13** and **13’** obtained from the SPAAC reaction between **1** and **5**



Major isomer **13**

Colorless solid; Mp 204 °C (decomp.); TLC R_f 0.43 (*n*-hexane/EtOAc = 1/2); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.53 (s, 3H), 3.90 (s, 3H), 4.32 (d, 1H, *J* = 16.5 Hz), 5.65 (d, 1H, *J* = 14.5 Hz), 5.70 (d, 1H, *J* = 14.5 Hz), 6.02 (d, 1H, *J* = 16.5 Hz), 6.93 (dd, 1H, *J* = 7.7, 1.0 Hz), 7.17–7.21 (m, 4H), 7.26–7.29 (m, 1H), 7.33–7.37 (m, 1H), 7.45–7.49 (m, 2H), 7.71–7.75 (m, 1H), 7.99–8.04 (m, 2H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 22.4 (1C), 51.3 (1C), 52.1 (1C), 52.3 (1C), 124.2 (1C), 127.0 (2C), 127.1 (1C), 127.5 (1C), 129.2 (1C), 129.7 (1C), 129.8 (1C), 129.9 (1C), 130.1 (1C), 130.3 (2C), 130.5 (1C), 131.2 (1C), 131.8 (1C), 135.0 (1C), 136.0 (1C), 139.9 (1C), 140.9 (1C), 143.1 (1C), 166.7 (1C), 170.6 (1C); IR (KBr, cm^{-1}) 754, 1020, 1110, 1280, 1392, 1433, 1508, 1664, 1721, 2949, 3059; HRMS (ESI$^+$) *m/z* 461.1586 ([M+Na]$^+$, $C_{26}H_{22}N_4NaO_3^+$ requires 461.1584).

Minor isomer **13’**

Colorless solid; Mp 238 °C (decomp.); TLC R_f 0.29 (*n*-hexane/EtOAc = 1/2); Compound **13**’ was observed as a mixture of conformational isomers in NMR analyses; ^{1}H NMR for major isomer ($CDCl_3$, 500 MHz) δ 1.17 (s, 3H), 3.91 (s, 3H), 4.41 (d, 1H, *J* = 16.7 Hz), 5.53 (d, 1H, *J* = 15.4 Hz), 5.77 (d, 1H, *J* = 15.4 Hz), 5.91 (d, 1H, *J* = 16.7 Hz), 7.16–7.18 (m, 2H), 7.23–7.41 (m, 6H), 7.51 (ddd, 1H, *J* = 7.7, 7.7, 1.5 Hz), 7.61 (dd, 1H, *J* = 7.7, 1.5 Hz), 7.99–8.04 (m, 2H); ^{1}H NMR for minor isomer ($CDCl_3$, 500 MHz) δ 1.99 (s, 3H), 3.94 (s, 3H), 4.96 (d, 1H, *J* = 18.1 Hz), 5.20 (d, 1H, *J* = 16.2 Hz), 5.46 (d, 1H, *J* = 18.1 Hz), 5.79 (d, 1H, *J* = 16.2 Hz), 6.87 (dd, 1H, *J* = 7.7, 1.5 Hz), 7.12 (d, 1H, *J* = 7.3 Hz), 7.23–7.41 (m, 6H), 7.51–7.54 (m, 1H), 7.74 (dd, 1H, *J* = 7.7, 1.5 Hz), 8.06–8.11 (m, 2H);^{13}C NMR ($CDCl_3$, 126 MHz) δ 21.2, 21.7, 51.5, 51.6, 52.2, 52.3, 52.9, 56.3, 127.1, 127.2, 127.3, 127.4, 127.5, 128.1, 128.4, 128.5, 128.6, 128.95, 128.98, 129.0, 129.3, 129.4, 130.1, 130.3, 130.4, 130.5, 131.5, 131.6, 131.8, 132.3, 132.70, 132.74, 133.4, 133.5, 139.9, 141.2, 142.2, 142.3, 143.5, 146.1, 166.3, 169.3; Some signals were not observed clearly due to the existence of conformational isomers; IR (KBr, cm^{-1}) 761, 1118, 1280, 1305, 1672, 1714, 2949, 3048; HRMS (ESI$^+$) *m/z* 461.1590 ([M+Na]$^+$, $C_{26}H_{22}N_4NaO_3^+$ requires 461.1584).

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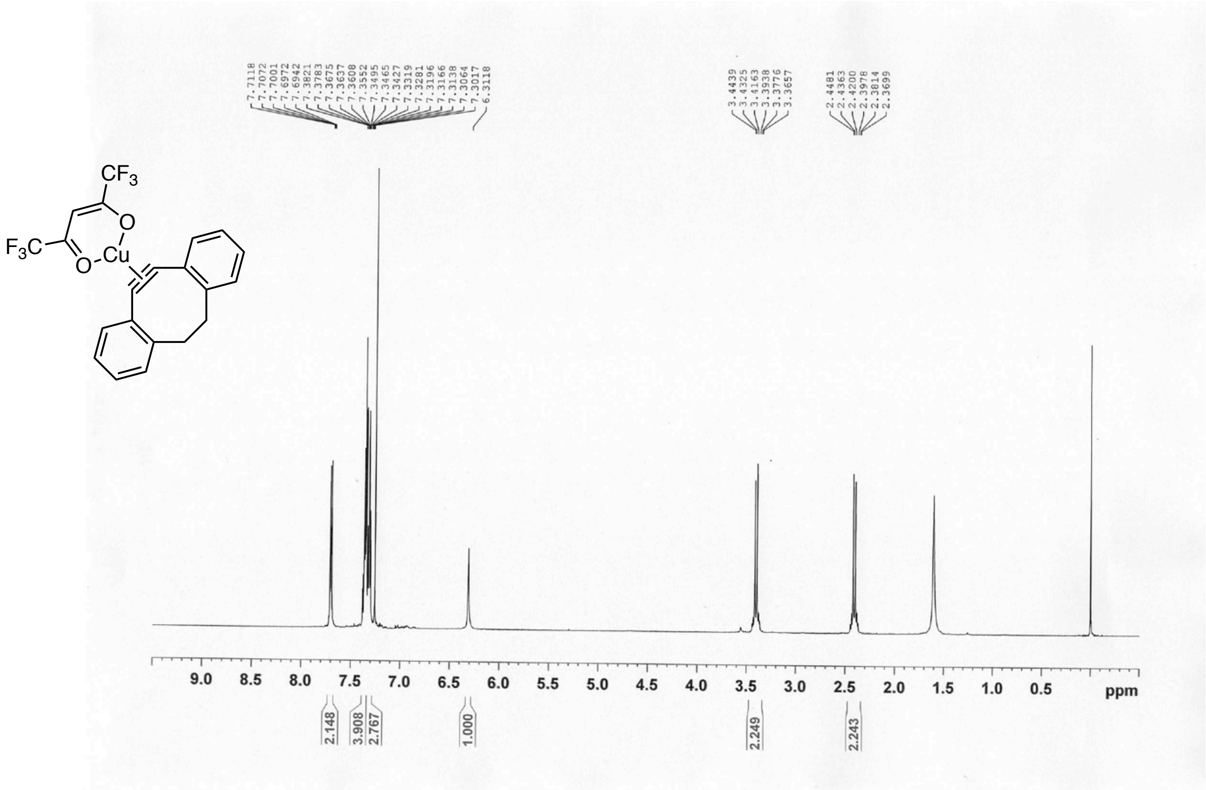
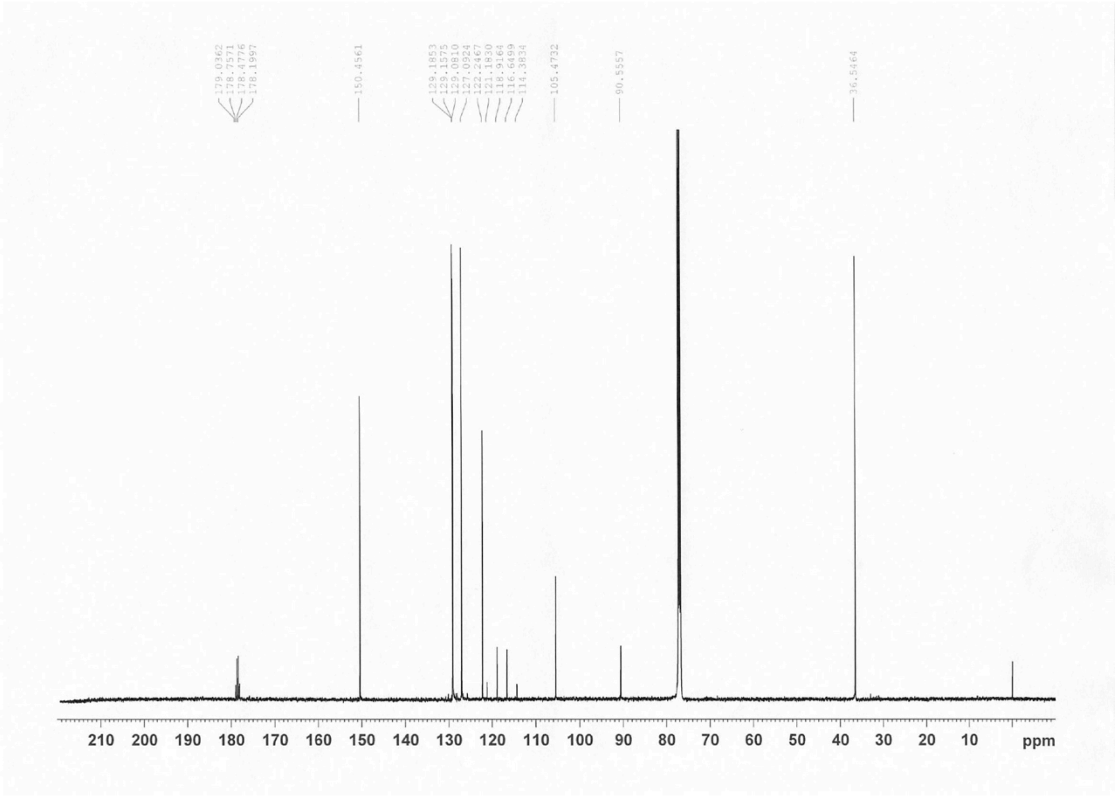
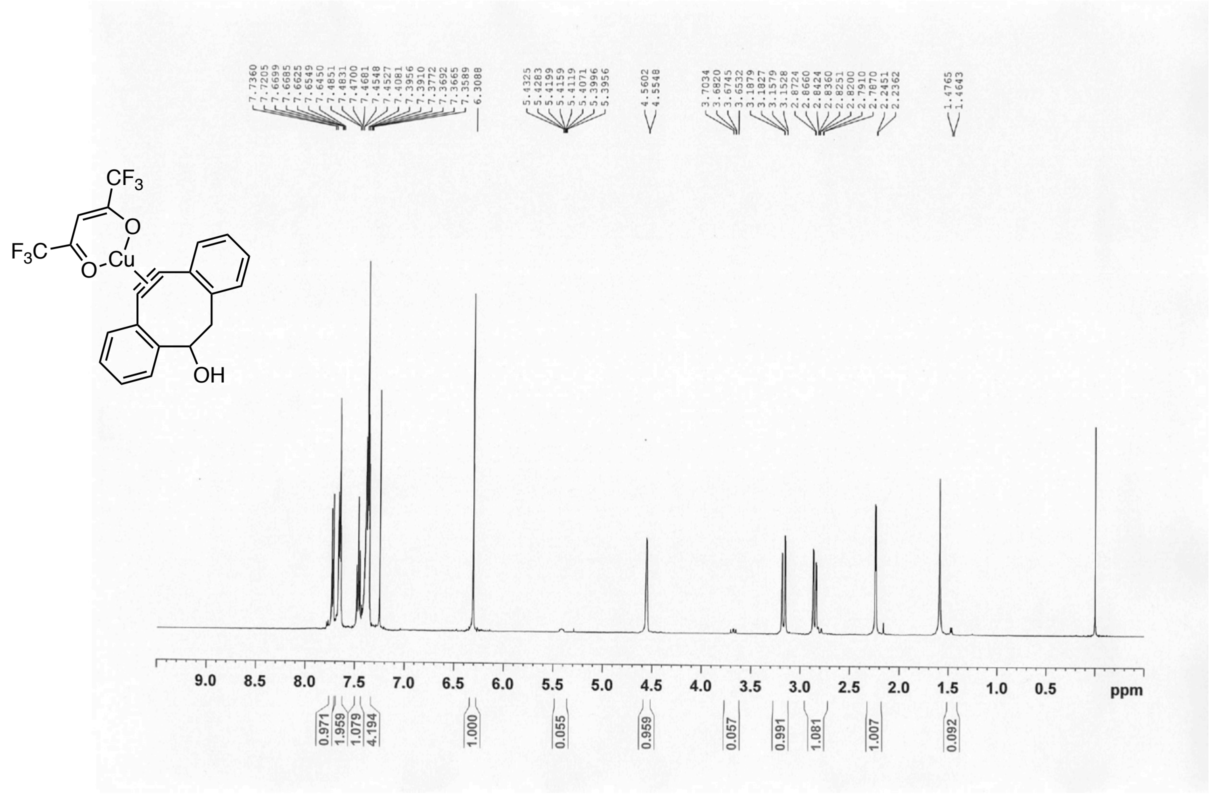
NMR Spectra of New Compounds

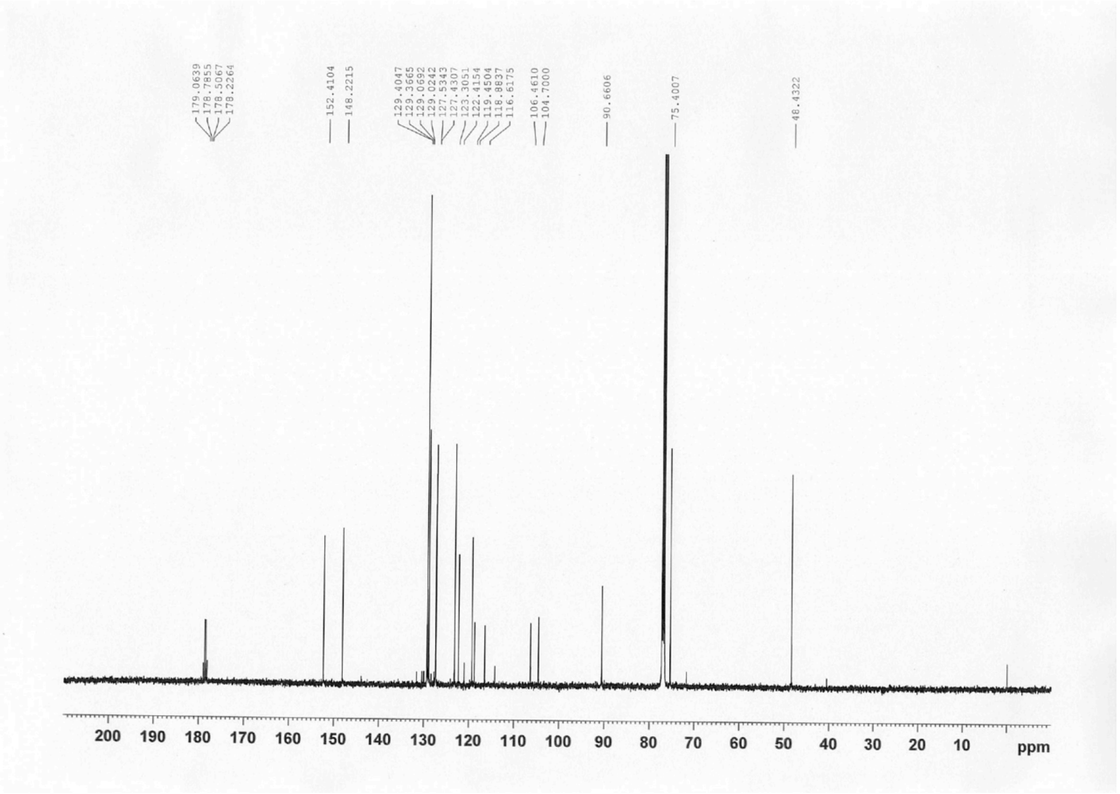
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of [5,6-didehydro-11,12-dihydrodibenzo[*a*,*e*]cyclooctene](hexafluoroacetylacetonato)copper(I) (**4a**) (CDCl$_3$)



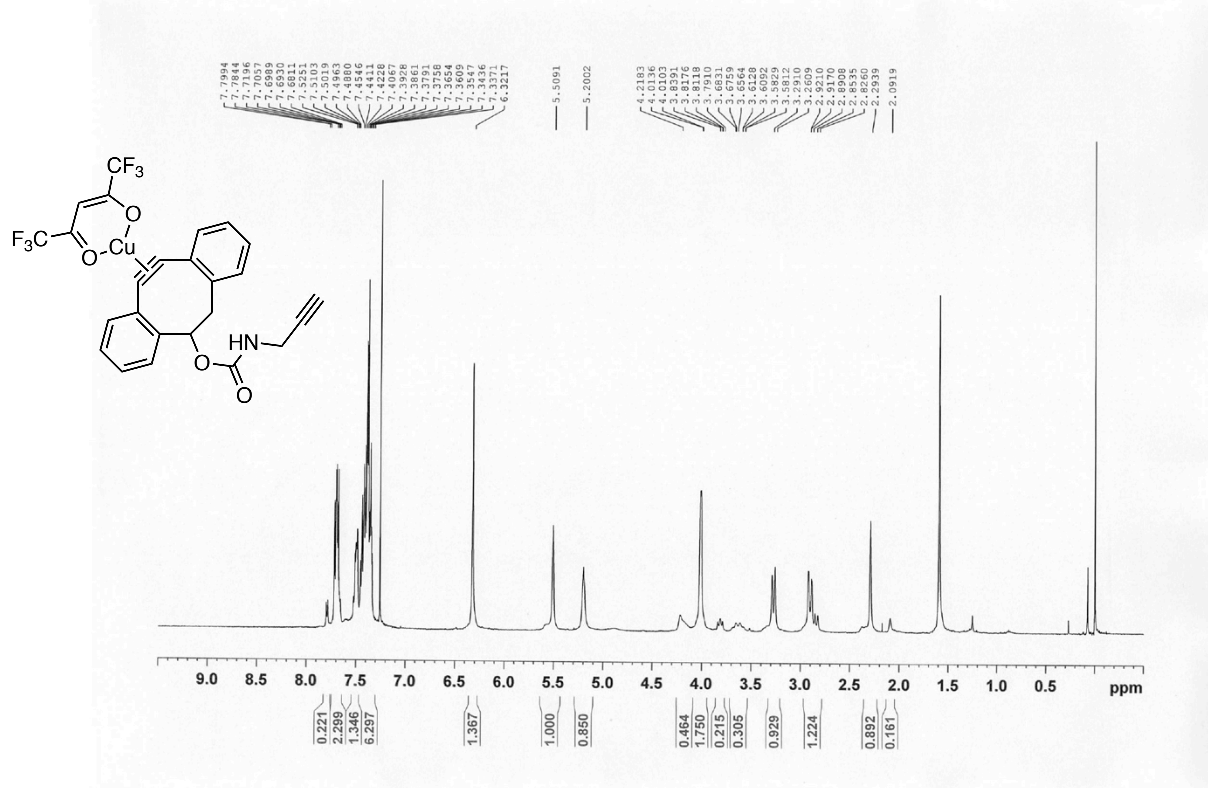


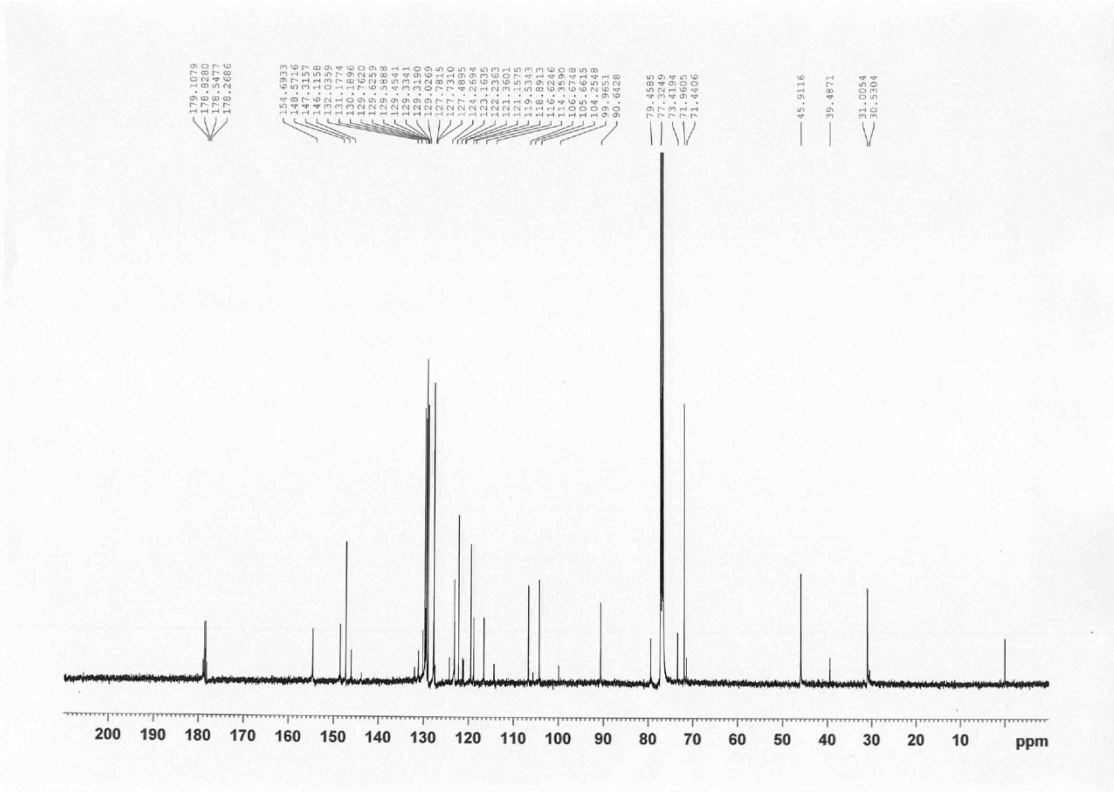
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of [11,12-didehydro-5,6-dihydro-dibenzo[*a*,*e*]cycloocten-5-ol](hexafluoroacetylacetonato)copper(I) (**4b**) ($CDCl_3$)



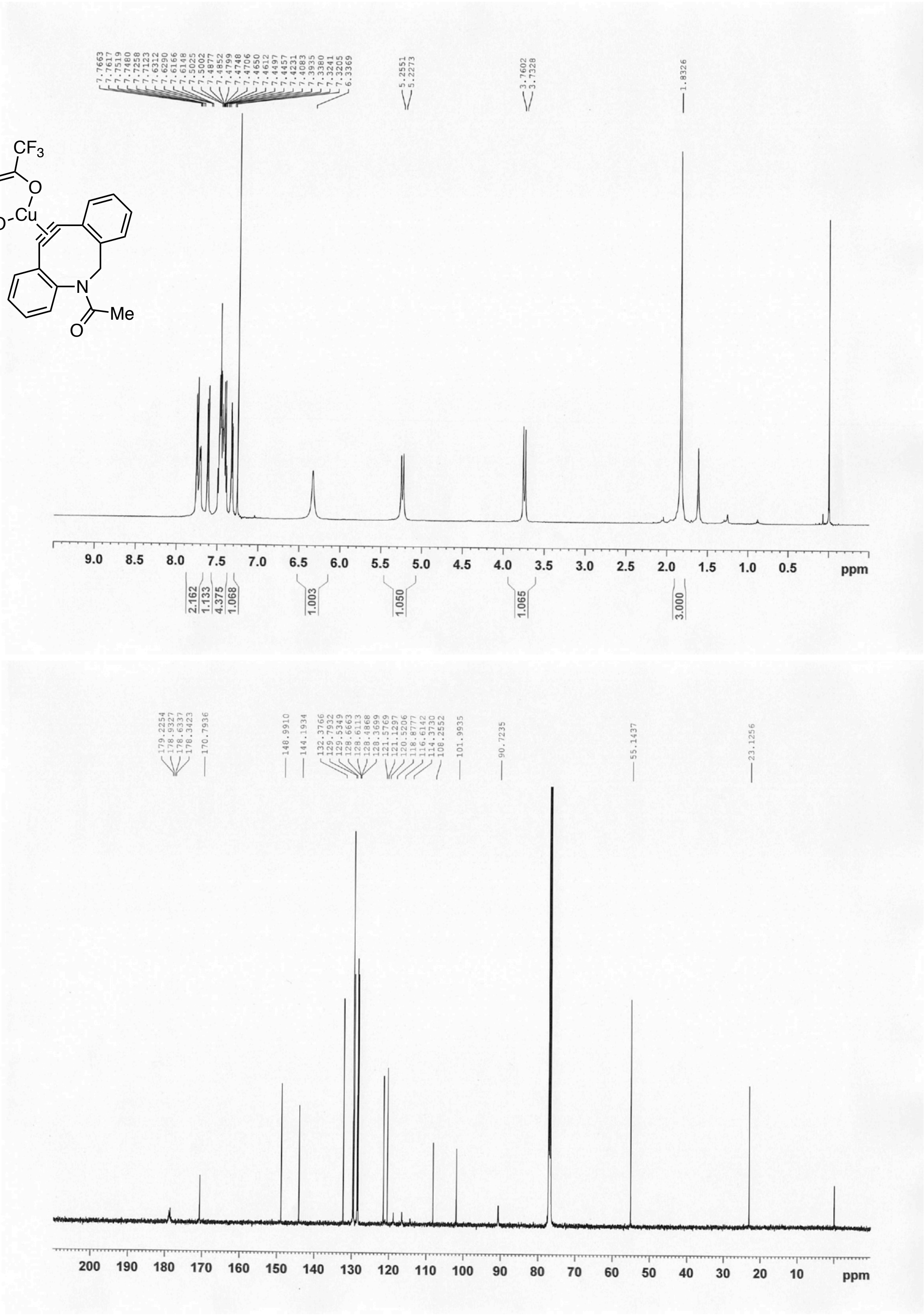


^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of [11,12-didehydro-5,6-dihydrodibenzo[*a,e*]cycloocten-5-yl *N*-(2-propyn-1-yl)carbamate](hexafluoroacetylacetonato)copper(I) (**4c**) ($CDCl_3$)

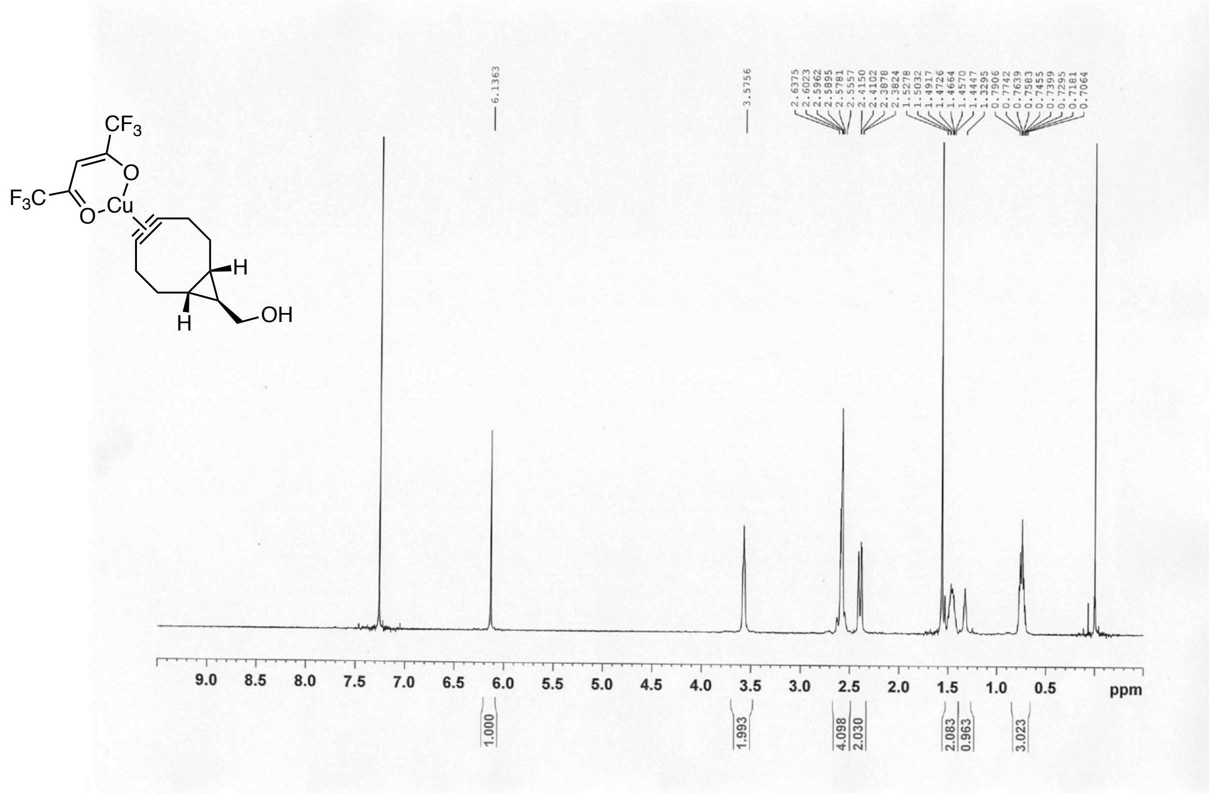


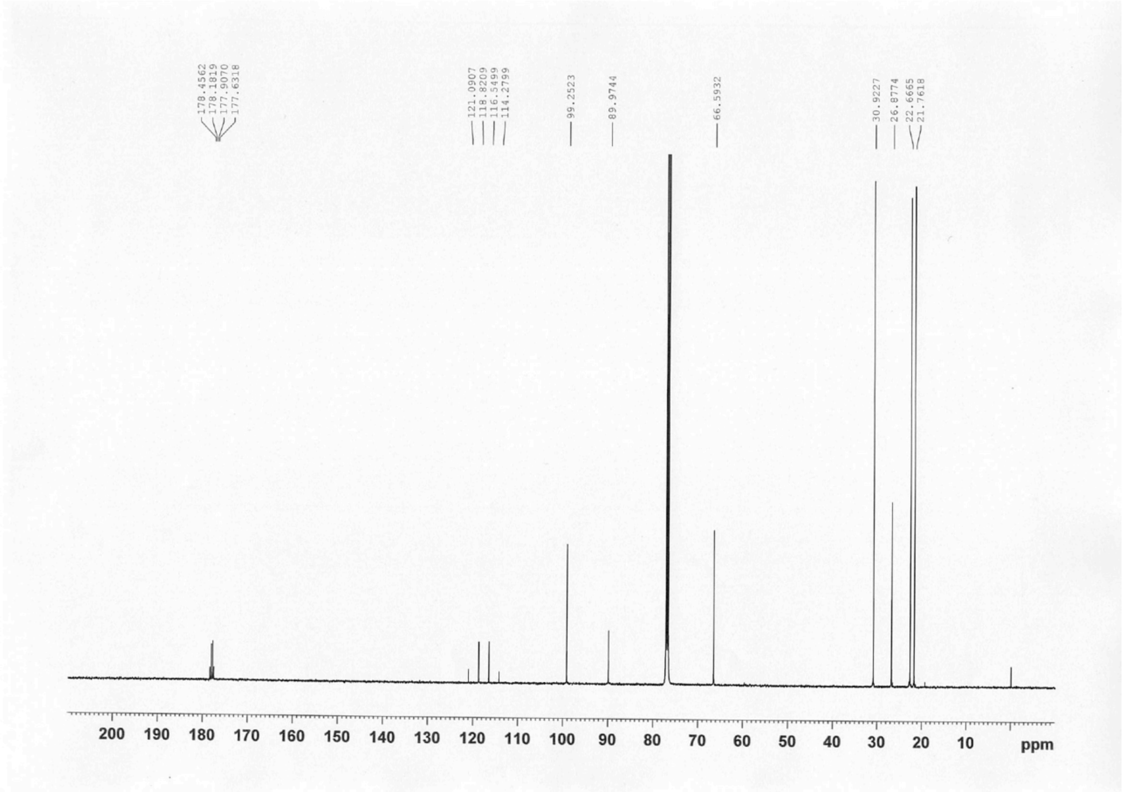


^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of [5-acetyl-5*H*,6*H*-11,12-didehydrodibenzo[*b*,*f*]azocin](hexafluoroacetylacetonato)copper(I) (**4d**) ($CDCl_3$)

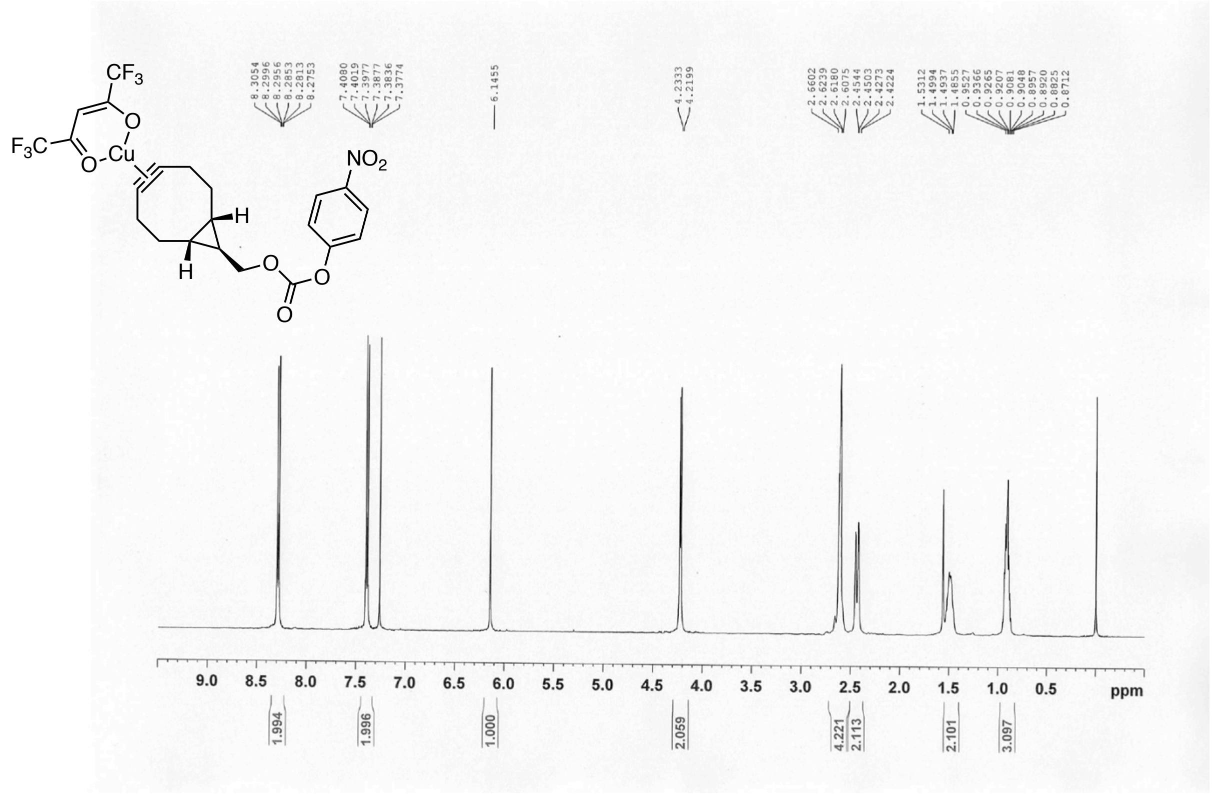


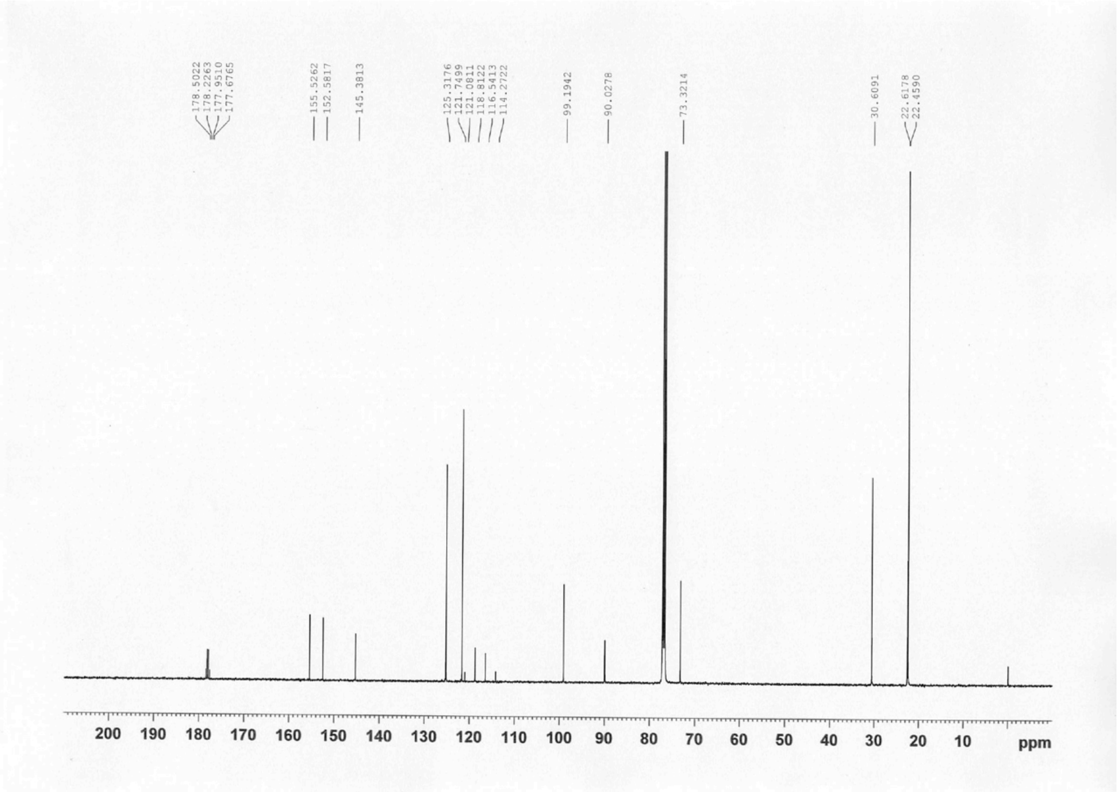
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of [(1α,8α,9α)-bicyclo[6.1.0]non-4-yn-9-ylmethanol](hexafluoroacetylacetonato)copper(I) (**4e**) ($CDCl_3$)



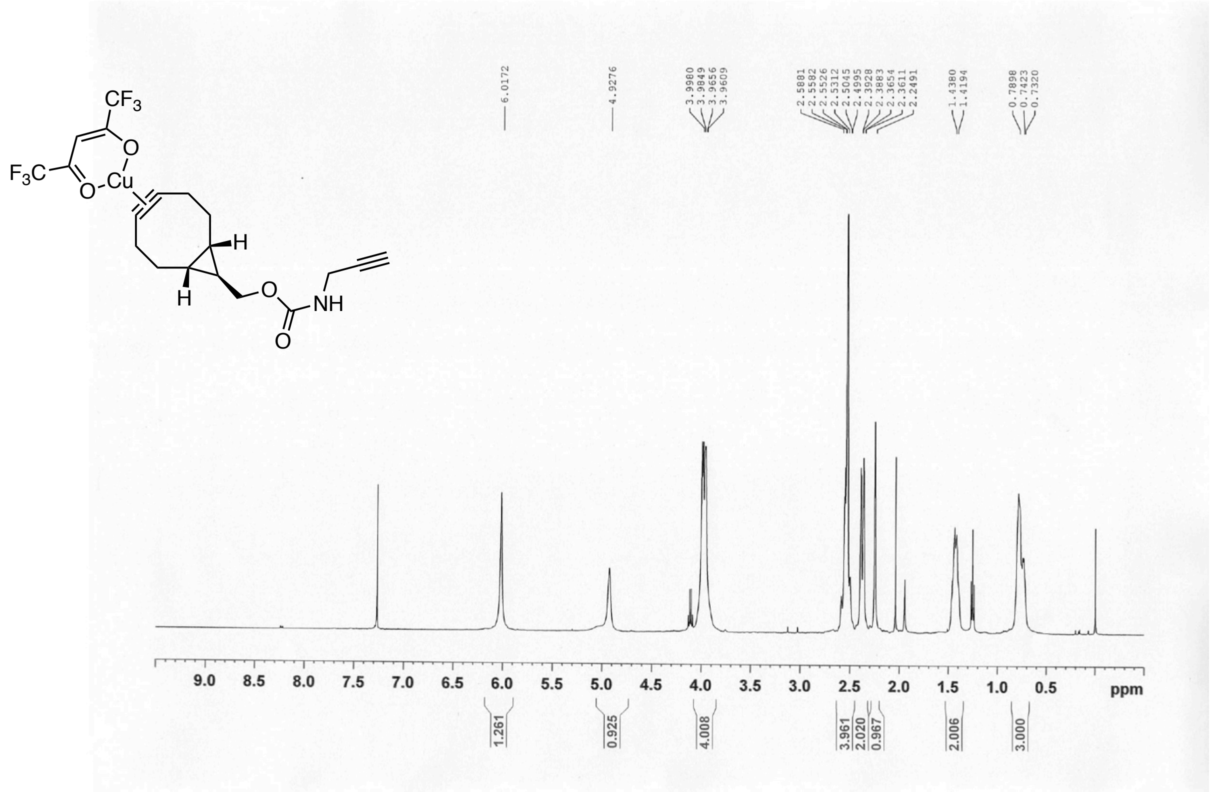


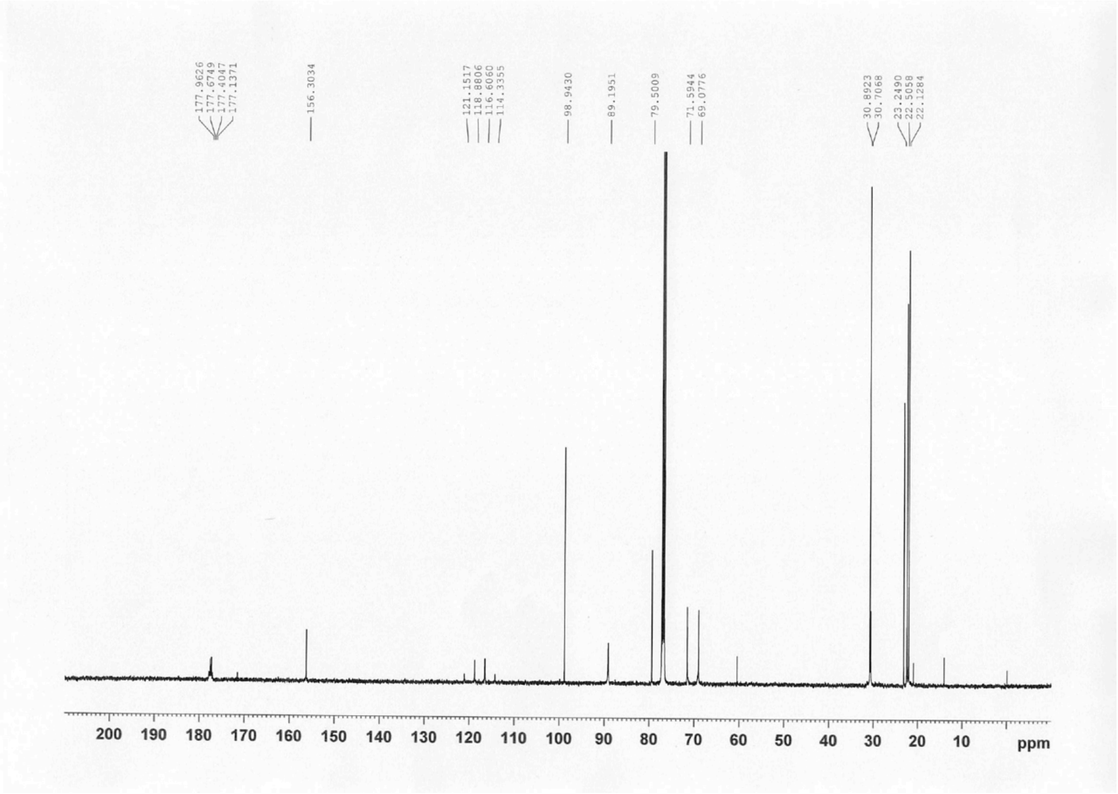
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of [(1α,8α,9α)-bicyclo[6.1.0]non-4-yn-9-ylmethyl (4-nitrophenyl)carbonate](hexafluoroacetylacetonato)copper(I) (**4f**) ($CDCl_3$)



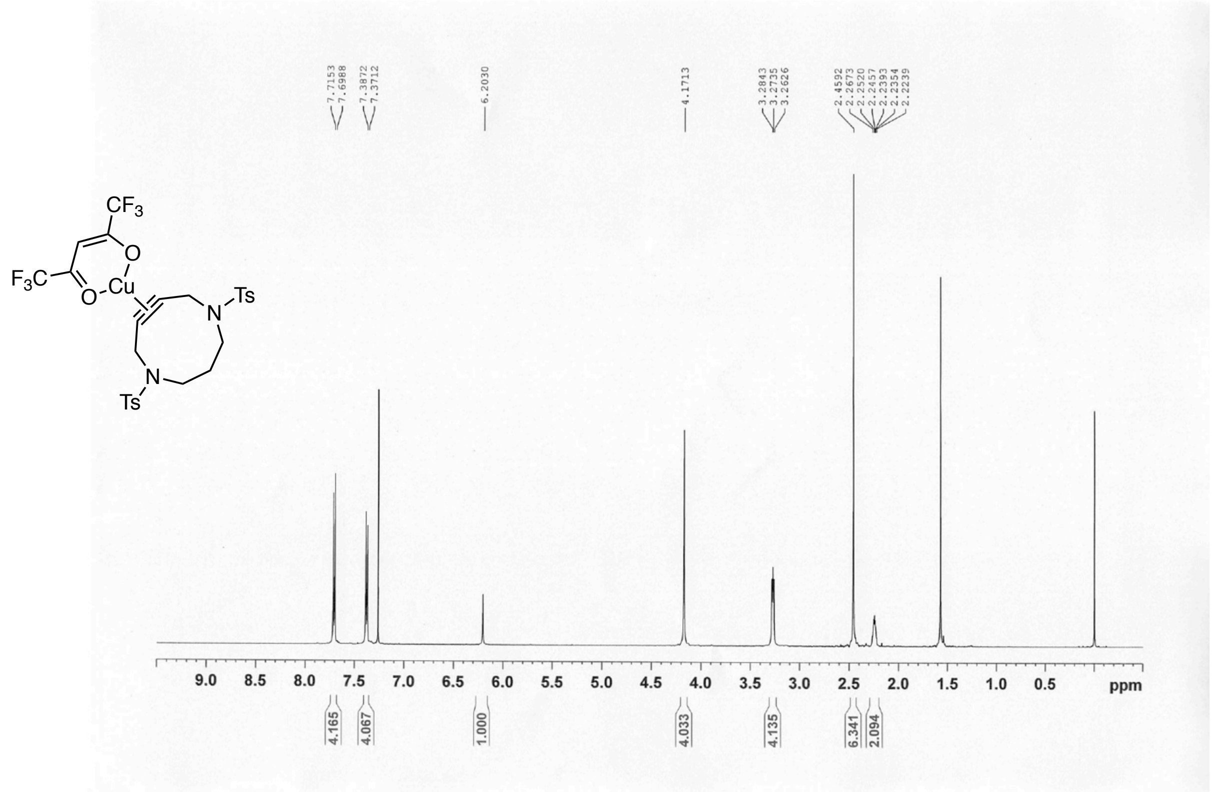


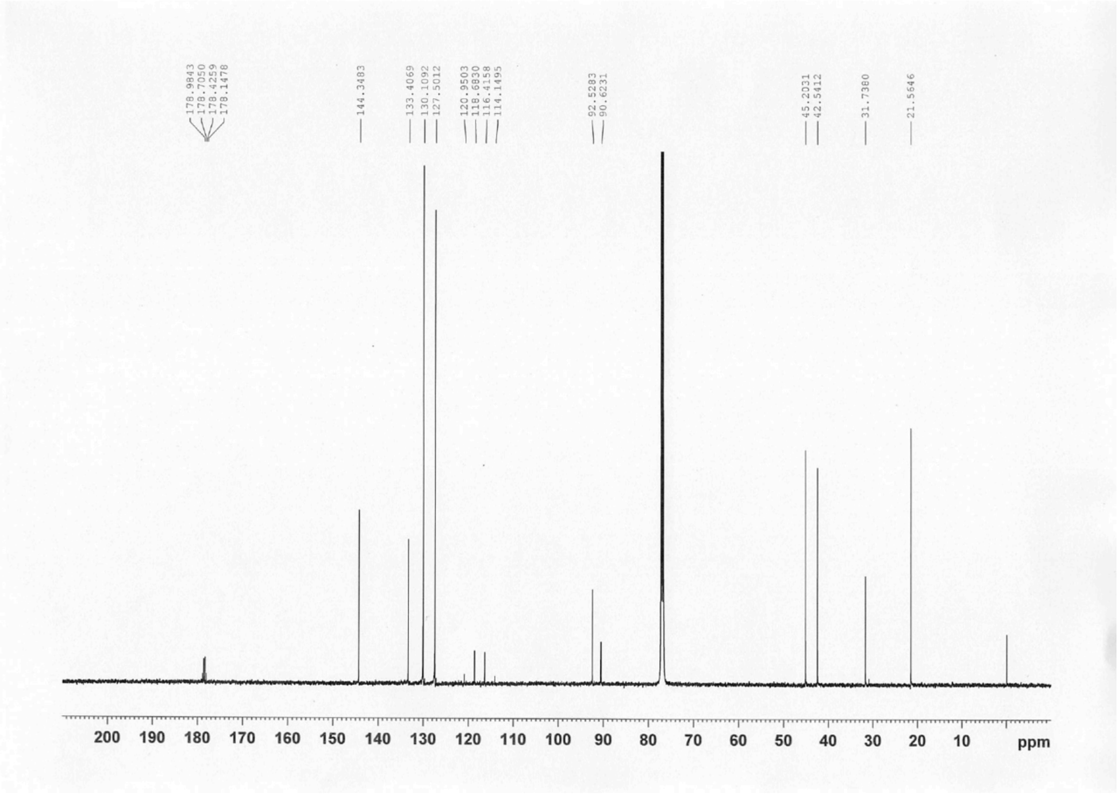
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of [(1α,8α,9α)-bicyclo[6.1.0]non-4-yn-9-ylmethyl *N*-(2-propyn-1-yl)carbamate](hexafluoroacetylacetonato)copper(I) (**4g**) ($CDCl_3$)



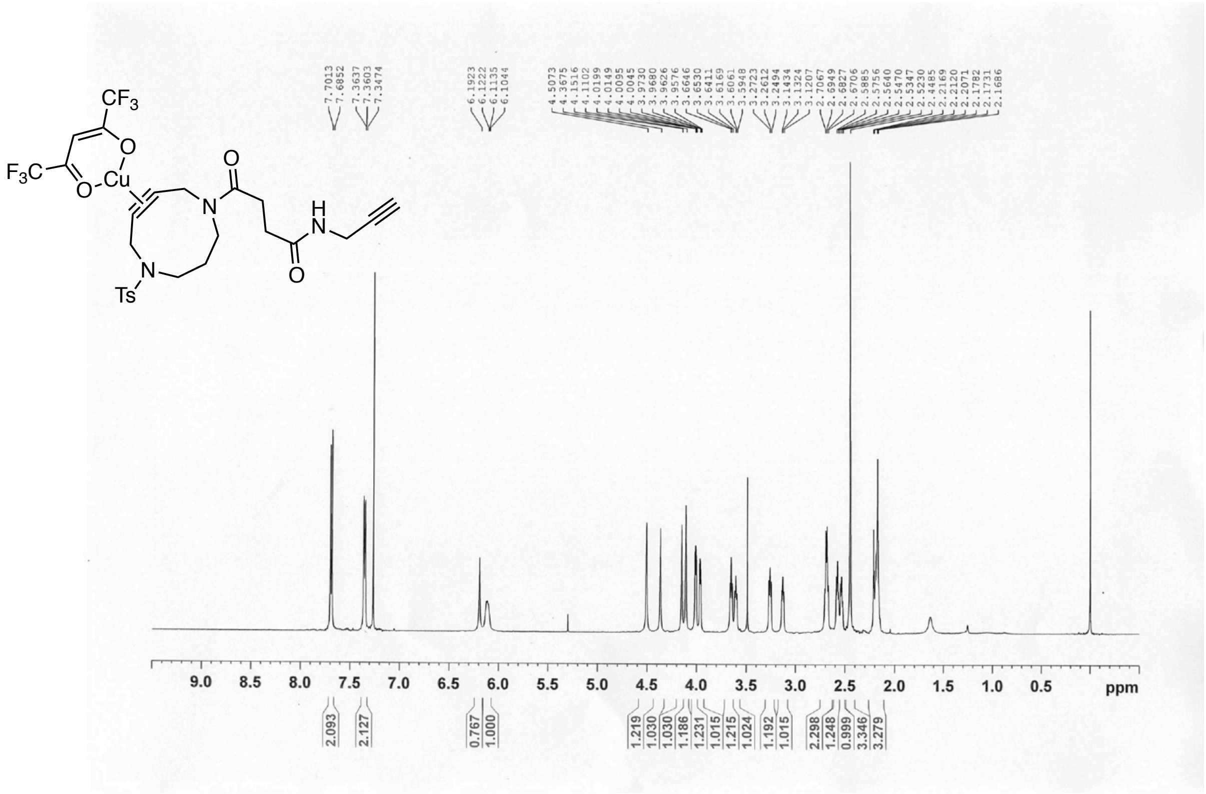


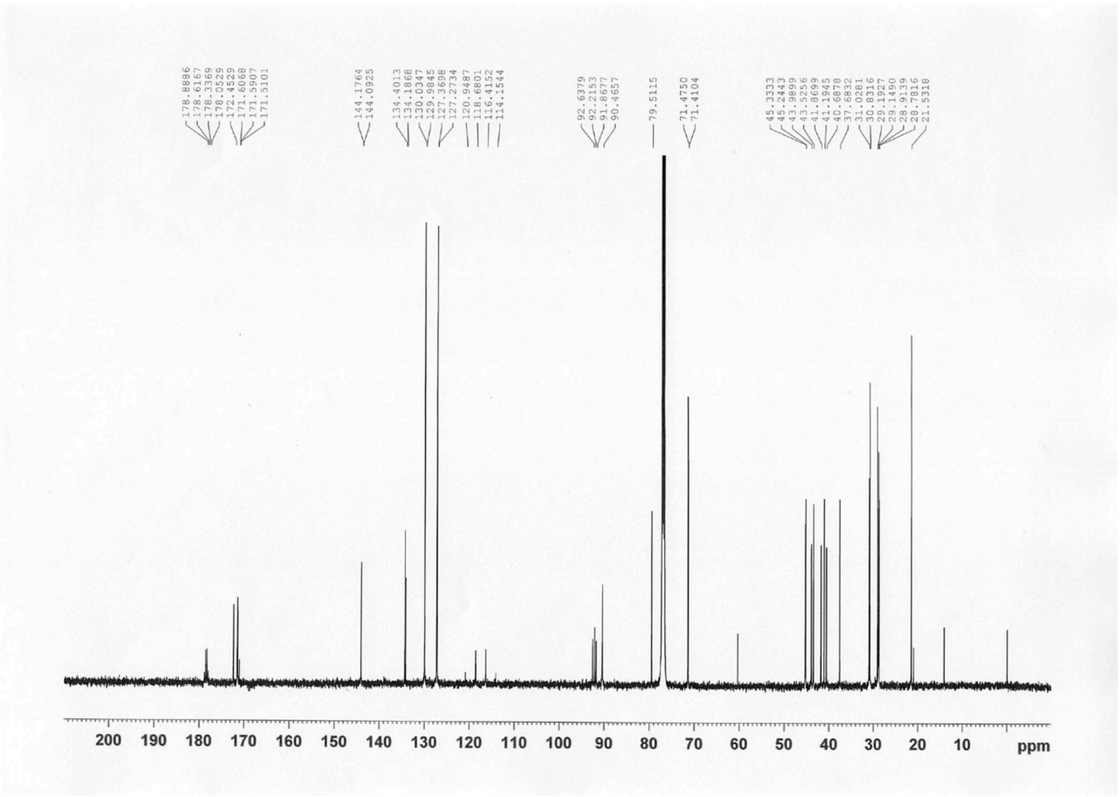
^1H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of [4,8-ditosyl-4,8-diazacyclononyne](hexafluoroacetylacetonato)copper(I) (**4h**) ($CDCl_3$)



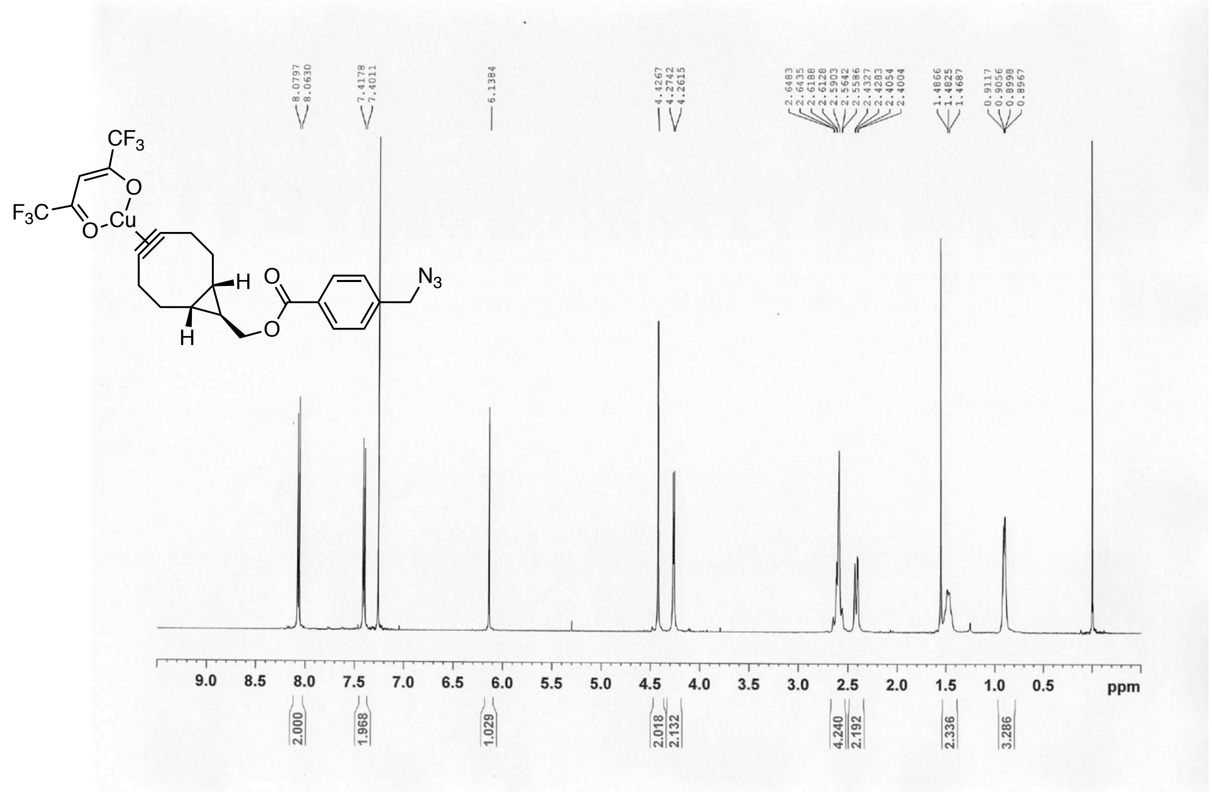


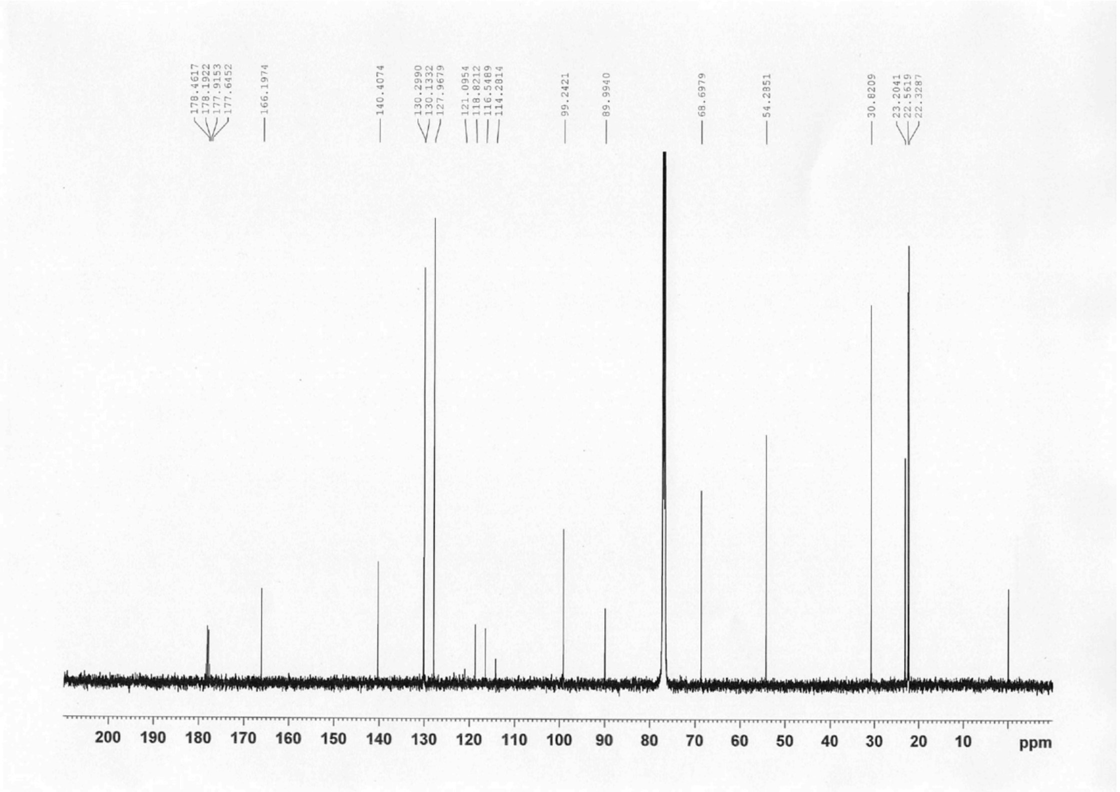
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of [3-(4-tosyl-4,8-diazacyclononyn-8-ylcarbonyl)propionamide](hexafluoroacetylacetonato)copper(I) (**4i**) ($CDCl_3$)



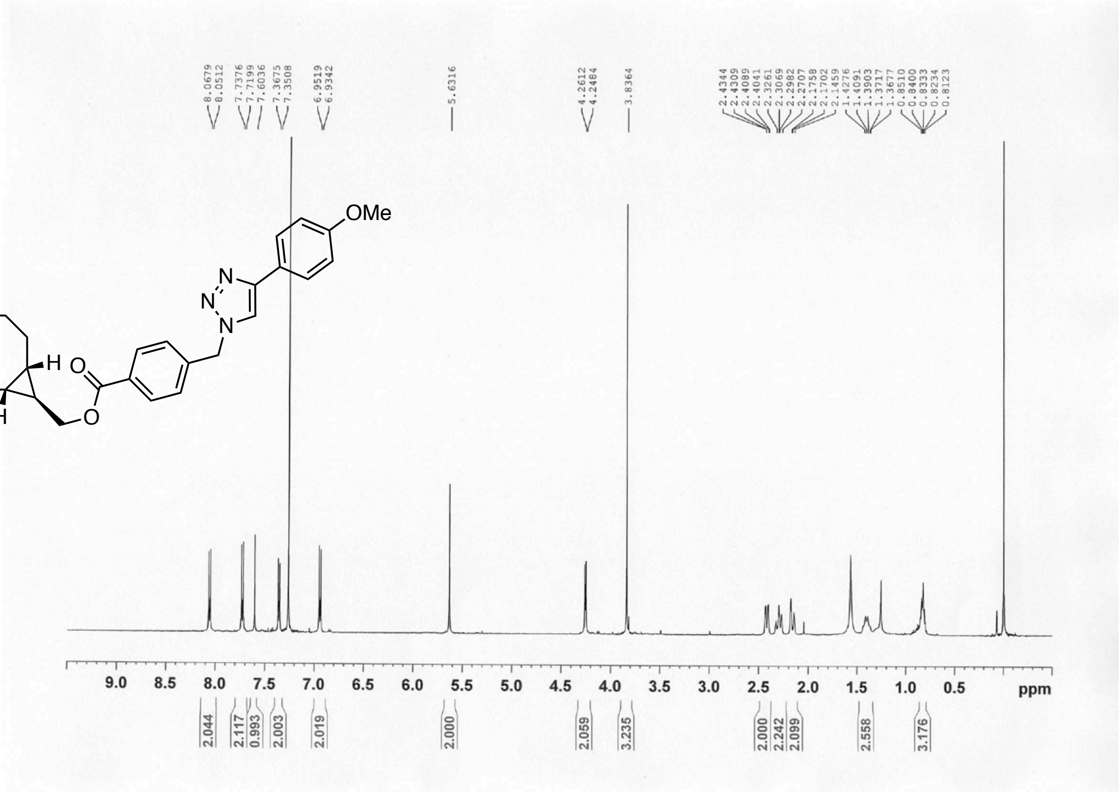


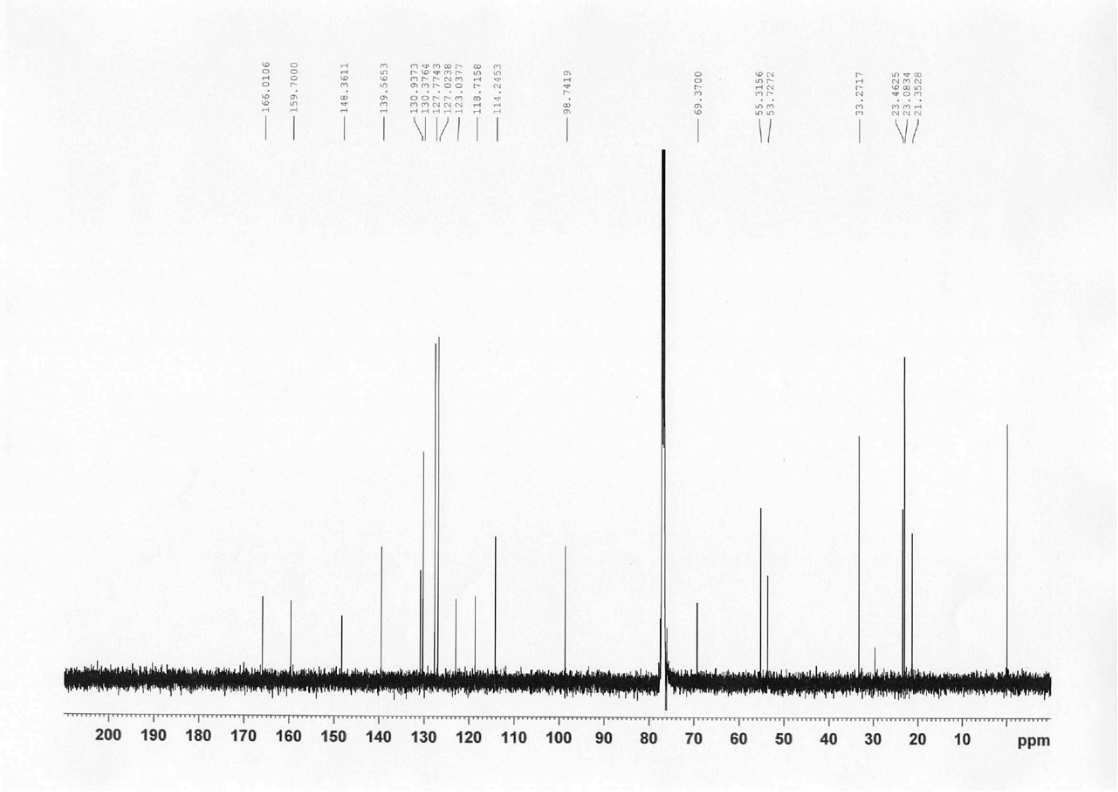
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of [((1α,8α,9α)-bicyclo[6.1.0]non-4-yn-9-yl)methyl 4-(azidomethyl)benzoate](hexafluoroacetylacetonato)copper(I) (**4j**) (CDCl$_3$)



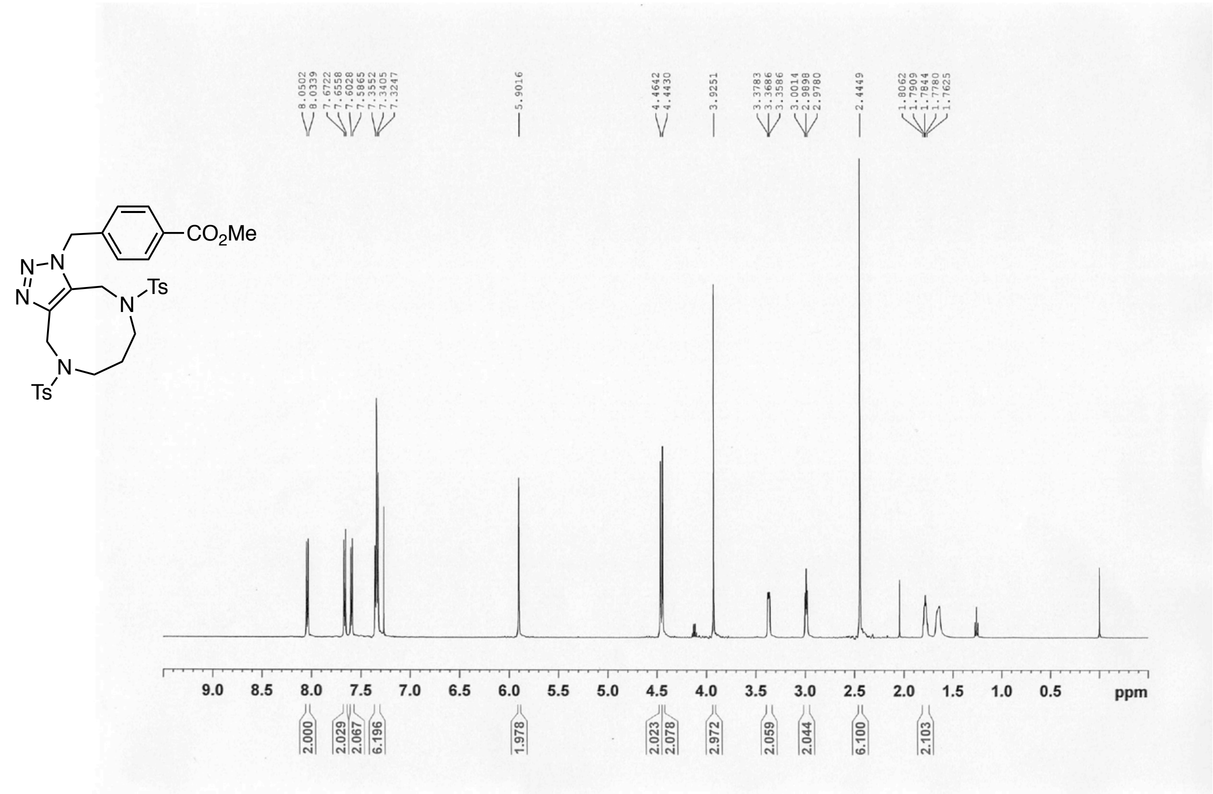


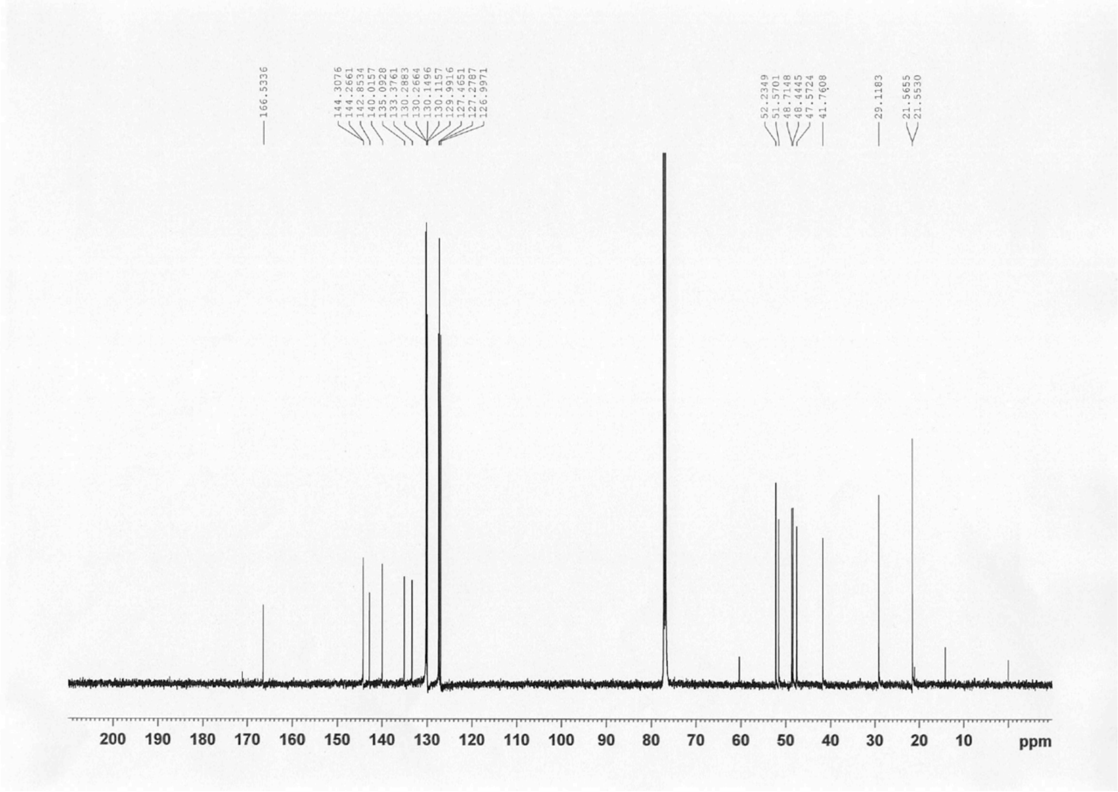
^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of ((1α,8α,9α)-bicyclo[6.1.0]non-4-yn-9-yl)methyl 4-((4-(4-methoxyphenyl)-1*H*-1,2,3-triazol-1-yl)methyl)benzoate (**9**) (CDCl$_3$)



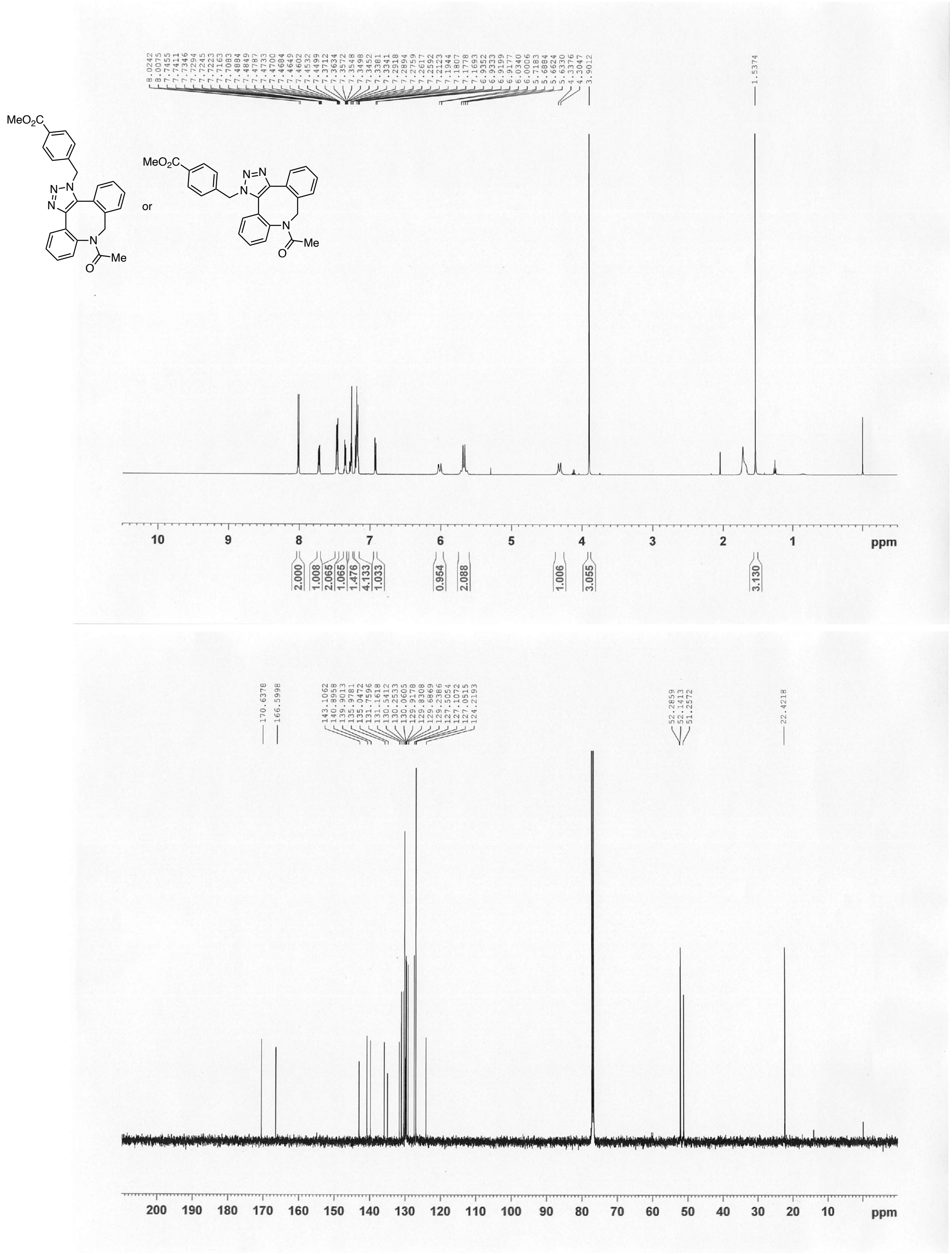


^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of methyl 4-((5,9-ditosyl-5,6,7,8,9,10-hexahydro-[1,2,3]triazolo[4,5-*g*][1,5]diazonin-1(4*H*)-yl)methyl)benzoate (**12**) (CDCl$_3$)





^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of major isomer (**13**) in the cycloadducts obtained from the SPAAC reaction between **1** and **5** ($CDCl_3$)



^{1}H NMR (500 MHz) and ^{13}C NMR (126 MHz) spectra of minor isomer (**13'**) in the cycloadducts obtained from the SPAAC reaction between **1** and **5** ($CDCl_3$)